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THE PHARMACOPEIA
AND
THE PHYSICIAN

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THE PHARMACOPEIA
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A Series of Articles which Originally Appeared in the Journal of the American Medical Association, Discussing the Chief Substances in the United States Pharmacopeia, Classifying Them According to Their Uses and Describing Their Methods of Combination and How They May Take the Place of Many Proprietary Preparations for Which Extravagant Claims Have Been Made.

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PREFACE TO THE SECOND EDITION

The nucleus of the material that now comprises the chapters of this book was originally compiled to assist in the introduction of the Pharmacopeia of the United States, its scope and contents and the possibilities and uses of official remedies, to the physicians of this country. While it is true that the Pharmacopeia itself may be considered as being, in a certain sense, a reference book on pharmacology, the information that it contains is not of a nature to indicate the various actions of the several drugs on the animal organism or to suggest the therapeutic uses of official remedies.

Schmiedeberg asserted, many years ago, that the proper function of pharmacology is to indicate the way, or to point out the material that is useful, to the clinician and not to give detailed directions for the therapeutic uses of the remedies themselves.

In the following chapters an earnest effort has been made to heed these limitations, and the compilers have endeavored to discuss, at times at some length, the more important and more reliable official remedies from a purely pharmacologic point of view, for it is now generally admitted that the pharmacologic action is the only reliable key to the therapeutic use of a drug. To the keen observer of matters medical it must be evident that the physician who has secured a firm grasp on the

possibilities and the limitations of medicinal substances, as indicated by their pharmacodynamic action, will not be misled either by the wily tales of the detail man or the all too frequently haphazard clinical observations made by overzealous fellow practitioners. A physician who has mastered the fundamentals of pharmacology will thoroughly appreciate that there can be no virtue in secrecy so far as drugs and medicinal substances are concerned, and will readily recognize the self-evident fact that all of the effects produced by esoteric combinations of well-known medicaments can, and must, be produced equally well by the use of the same medicaments under their proper designations.

With the gradual increase of our knowledge concerning the pharmacology of drugs there must be a corresponding decrease in the need, or the supposed need, for the empiric use of complex mixtures of either known or unknown composition, and the future medical practitioner will be in a position to evolve a comprehensive system of drug therapeutics from an intimate knowledge of the pharmacology of but a limited number of drugs and will, therefore, be free to ignore the use of all nostrums or ready-made prescriptions.

The first reprint of the original articles, in book form, was in the nature of an experiment, and it is particularly gratifying, therefore, that a second edition is needed at this time. The rapidity with which the first edition was sold evidences a healthy spirit of inquiry on the part of medical practitioners, and is no doubt indicative of an honest attempt on the part of many older men in the

medical profession to break away entirely from the use of secret or proprietary nostrums and confine themselves more and more to open formulas and official preparations.

The compilers of the material herewith presented are, however, desirous of doing even more than this. They are anxious to awaken a more widespread recognition of the fundamental principles of a rational materia medica based on demonstrable action of medical substances on the animal organism. They feel that with a proper appreciation of the possibilities of the science of pharmacology the practice of medicine can rid itself of the overconfidence of the more credulous in complex specifics, and also rid itself of the last vestiges of therapeutic nihilism, real or imaginary, that is now evidenced by the practices of some of the more skeptical. In place of the really unsatisfactory conditions of to-day we may look forward then to a healthy spirit of optimism based on the demonstrable action of substances of definite composition.

The compilers wish to lay particular stress upon the obligation which every man owes to his profession—the duty to transmit, unimpaired, the knowledge of the action, and comparative value of therapeutic agents, which he has received as the result of past experiences, with the added weight of his own experience based on intelligent observation. This is wholly impossible with those who take up and follow the cry put into their mouths by wily makers of nostrums—"I will use anything that helps my patients." Such an obviously correct procedure is made the excuse for using anything

that is *said* to help the patient, which is very commonly the exact opposite of what the original saying proclaims.

It is extremely difficult to know what will help our patients at times, but it is never difficult to find scores of remedies which are *said* to help any given condition. When carefully analyzed this frequently-heard cry is found to be an obviously shallow expression, as it presupposes infinite therapeutic and pharmacologic knowledge. If it is followed with nostrums as a basis we must soon come to the point of utter confusion so far as experience is concerned, for the nostrum exists but a day, until another, more blatantly advertised, replaces it.

One really great evil which pertains to the nostrum traffic, and one which is not usually considered, is the deliberate attempt to misrepresent and belittle the value of thoroughly well established official remedies. If a manufacturer attacks the products of a rival a counter attack will let in too much light for the good of either, hence there is a mutual regard, or at least tolerance, established between nostrum makers, but it appears that no one is particularly interested, at least financially, in the official materia medica, and attacks may be made on official articles with impunity. With the individual practitioner this species of attack frequently leads him to overlook, or to ignore entirely, his heritage of the knowledge of the therapeutics of official articles, sometimes the result of centuries of experience, and to lend an all too willing ear to the claims of the nostrum maker, only to find that he has been misled and that, through him, his pa-

tients have been deprived of the advantages of past experiences to which they were rightfully entitled.

The following simple rules of prescribing have been formulated by Torald Sollmann and are well worth careful consideration:

1. Do not use any new substitute (except in the way of scientific experimentation) unless it possesses distinct advantages over the older remedies.

2. Do not use a ready-made mixture in conditions which require individual consideration.

3. Do not prefer monopolistic proprietary remedies to official drugs.

THE PHARMACOPEIA AND THE PHYSICIAN.

INTRODUCTION.

The Pharmacopeia of the United States of America has been the generally accepted authority and the professed guide of American medical men, in matters therapeutic and pharmaceutic, for over eighty-five years. Since the publication of the first edition, in 1820, the book has undergone eight decennial revisions and to-day it is universally conceded to be the peer of authoritative books of its kind, for its scientific accuracy as well as for the general excellence of the descriptions and directions that it contains.

This recognized superiority of the Pharmacopeia of the United States of America, in its own particular field, and its generally accepted authority, as a guide, in all matters relating to the strength and purity of the medicinal articles enumerated in its pages, is all the more remarkable in that previous to the enactment of the Food and Drugs Act, June 30, 1906, it had never been granted a general recognition by statutory laws.

This lack of legal recognition has undoubtedly been a disadvantage to the book in so far that, in the past two decades at least, the contents, and even the very existence, of such an authoritative

book have been largely lost sight of by American physicians, and official remedies have been eclipsed to a very marked degree, or overshadowed by the innumerable patented and proprietary remedies that are constantly brought to the attention of medical men in the advertising material with which their offices are regularly deluged.

With a view of bringing the Pharmacopeia itself, its scope and its contents, more prominently before the medical profession, it is proposed to present, in the following chapters, a collection of facts and suggestions bearing on the number and variety of therapeutic indications that may be fully met with official drugs and preparations.

It is also proposed to call attention to the unreasonable claims and the extraordinary statements that are frequently made in connection with some of the arbitrary combinations of drugs that are offered as proprietary remedies or "patent" medicines, and to compare the probable limitations of these self-styled panaceas with the possible application and the varied uses of the more simple, and therefore more generally reliable, official remedies, the composition as well as the purity of which can be readily determined by well-known and easily applied methods.

It must be admitted that even the most recent, the eighth decennial, revision of the Pharmacopeia is not free from errors of commission and omission, but many of the shortcomings that are usually attributed to the book are really due to the general lack of interest that has been displayed by

physicians; and these shortcomings will be corrected in future revisions, if members of the medical profession will only make their needs and wishes known at the proper time and place.

It has been repeatedly asserted that the Pharmacopeia of the United States is designed primarily for pharmacists and for the manufacturers of pharmaceutical galenicals, and that it contains little or nothing of direct interest to the physician. One of the prime objects of the following chapters is to demonstrate that this assertion embodies only a half truth and that the present edition of our national Pharmacopeia really contains much that should interest every physician.

In this connection it should also be remembered that the technical descriptions and tests, for which the average physician may think he has little or no use, are in reality essential to secure for him and his patients, remedies that are not only reliable, but which are also uniformly active.

The leaders in American medicine have contributed so little to the evolution and advancement of the Pharmacopeia of the United States of America during recent decades, that it will be interesting, if not surprising, to many, to be reminded of the fact that the inception and inauguration of the Pharmacopeia are to be accredited to the leading minds in the medical profession of this country about eighty years ago.

Lyman Spaulding suggested the first practicable plan for securing a national Pharmacopeia at a

[illegible] being revised and discussed. In addition to having short descriptions of the physical properties of drugs, both whole and powdered, this Pharmacopœia has included doses, and, what is even more, has included short, suggestive remarks on the "Medicinal Operations" or therapeutic properties of the several drugs that were included in the text.

This edition of the Pharmacopœia was superseded, however, by the revision published under the direction of the convention which met in Washington in the same year, and which retained all of the features of the first edition.

Many factors have contributed to the loss of interest in the Pharmacopœia by medical men; among the more influential of these factors has been the general mistake of confusing the identity of the Pharmacopœia with that of the several Dispensatories which have been published, and, latterly at least, the apparent superfluity of any authority by the claimed superiority of new or proprietary remedies over the drugs and preparations of the Pharmacopœia.

With the advent of the new century, there appears to have been a re-awakening on the part of the members of the medical profession, and the interest that has been manifested in the work of the Council on Pharmacy and Chemistry of the American Medical Association, the articles that have appeared in lay journals on the abuse of nostrums by the laity and, last but by no means least,

the enactment of the Federal Food and Drugs Act, have all contributed to a renewed interest in true and tried remedies—an interest the authors of the following chapters have endeavored to enlarge upon and to foster.

THE USE OF EXTRAPHARMACOPEIAL SUBSTANCES AND THE NATIONAL FORMULARY.

A review of the application and the uses of pharmacopeial articles should be supplemented by a discussion of permissible extrapharmacopeial substances, and at least a passing reference to that most legitimate of all sources for extrapharmacopeial preparations—the National Formulary.

To appreciate more thoroughly the need for authoritative works of reference on extrapharmacopeial preparations we must remember that the remedies which have been properly included in the National Pharmacopeia constitute but a very limited portion of the possible resources of medical men of the present day, and are practically confined to those well-known drugs and preparations that are generally used in all parts of the country, and may, therefore, be considered as being thoroughly well established.

Despite the fact that a medical practitioner who is thoroughly well acquainted with the established, or official, materia medica is in a position to meet nearly all physiologic as well as therapeutic indications, so far as known, there is no gainsaying the fact that there can be no progress without experimentation, and experimentation in the field of

materia medica implies the use of new remedies in comparatively well understood pathologic conditions, or the use of established or otherwise well understood remedies in conditions that are less well understood.

With the gradual increase of our knowledge of the physiologic action and the limitations of medicinal substances there is a correspondingly decreasing need for the empiric use of, or the haphazard experimentation with, drugs and other therapeutically active substances. On the other hand, it must also be remembered that physiologic indications, as we understand or interpret them at the present time, do not fully represent the therapeutic uses and the limitations of medicinal substances in the diseased human organism.

Bearing in mind, then, the imperfect state of our knowledge concerning the normal functions of the several organs of the human body, the possible irregularities or diseases and the treatment of these irregularities with the more or less imperfect materials at our command, and the demands on the general practitioner in the daily routine, no reasonable individual can possibly object to the use of safe and well-understood substances that have been demonstrated to possess medicinal virtues, though they have not been admitted to the roll of more thoroughly established articles represented by the Pharmacopeia. Here, however, differences of opinion will arise as to what constitutes a safe and well-understood medicinal substance. Since it is

impossible for a medicinally active substance to be potent only for good and to be innocuous as far as deleterious results are concerned, we must modify the first part of our requirements and limit it to articles, the action and uses of which have been established.

While this requirement would undoubtedly constitute a reasonable and rational safeguard, it will be difficult to limit ourselves to it too strictly. The reasons for this will become more evident when we remember that such a comparatively simple drug as squill, which has been in continuous use for hundreds of years, even now is not well understood, either chemically or physiologically, and that digitalis, a drug that has been studied by the leading men in the medical profession almost continuously for half a century, still presents problems, both to the clinician and the pharmacologist.

When we realize how little positive knowledge we possess of the action, uses and limitations of drugs and medicinal preparations that have been in continued use for a long period of time, we begin to suspect that many of the positive claims that are now being made in connection with new drugs and medicinal preparations that have been after more careful observations, be found to be far from correct.

The secondary or so-called untoward effects of many drugs and preparations are so insidious that much harm may be done before it becomes known that such untoward effects should be looked for.

As an illustration of the harm that may result from the indiscriminate use of even the comparatively few new remedies that appear to have established themselves as permanent additions to our materia medica, attention is directed to the harm that has been done, both directly and indirectly, by acetanilid.

For over twenty years acetanilid was freely used, either in substance or in the form of various mixtures that are even now being marketed as proprietary nostrums. All of these preparations were presumed to be potent factors for good and innocuous so far as any deleterious results were concerned.

Despite the fact that many physicians suspected that acetanilid was directly responsible for a long train of little-understood symptoms, that occur as complications secondary to its excessive or continued use, it is fair to presume that but few were prepared to assert that acetanilid was directly to blame for so many really serious complications, and even deaths, as have been reported during the past few years.

Of the other new remedies that are widely used, largely because manufacturers have asserted that they are free from possible injurious effects, we may refer to the widely used coal-tar hypnotics. Drugs of this kind are freely used by lay persons, of all degrees of intelligence, in the mistaken belief that they are safe and harmless. It is known, however, that all hypnotics conduce to the con-

tinued use of sedative drugs and many are the direct cause of physical, mental and moral degeneracy. In addition to the possible harm that may result from the continued use of drugs of this type, it has been repeatedly shown that the coal-tar hypnotics, despite their reputed harmlessness, have been the direct as well as the indirect cause, of death in many instances.

One more illustration of our overzealousness to believe the assertions of manufacturers, to our own discredit: A few years ago diacetylmorphin, better known by the proprietary name heroin, was being exploited as a perfectly safe and reliable substitute for morphin. Heroin was reputed to possess all of the good properties of morphin without any of its faults, and it was even heralded as a positive cure for the morphin habit. According to more recent reports, however, heroin induces a habit as persistent as that caused by morphin.

The experience that we have obtained from these now better understood, and admittedly valuable, remedies should be sufficient to make us more cautious in the use of new drugs and chemicals that are exploited by those whose only interest is commercial. The most evident need in connection with the introduction of new drugs and chemicals is more information bearing on their untoward results and shortcomings, so that unnecessary repetition of disappointing and at times harmful experiences may be avoided. How imperative is the need for greater publicity in connection with newer

remedies is well illustrated by the volumes that have been published about them during the past two decades. If we examine one of the volumes published ten years ago we find hundreds of highly recommended substances that are now out of use, despite the fact that no derogatory report can be found in the pages of current medical journals. It is evident that some vital reason exists for the disappearance of these substances, but the present method of eliminating such new remedies is objectionable because it is slow and harmful to our patients.

The publication of the Handbook on New and Non-official Remedies by the American Medical Association, through its Council on Pharmacy and Chemistry, will no doubt contribute materially to bring about a better understanding and a more rapid elimination of the numerous remedies of uncertain value and composition that are now being offered. In this connection it is fair to suppose that manufacturers who will be given the advantage of added publicity, for the desirable properties of their several preparations, will not oppose free and impartial discussion of the shortcomings and the limitations of the same preparations.

Drugs and chemicals of original and meritorious character constitute but one of several classes of extrapharmacopeial articles that merit careful consideration. A much larger class, and one whose use has been accompanied by even greater abuses, consists of mixtures of more or less well-known

substances whose preparation requires only ordinary pharmaceutical skill and which may be prepared quite as satisfactorily by the retail pharmacists as by the large manufacturer. The allegations that are usually made for mixtures of this kind, when exploited as proprietary products, are frequently misleading, due to the misstatements that are made by their manufacturers.

Another cause for the present situation is the assumption by many manufacturers that the simple admixture of two or more well-known substances constitutes a discovery, and that the making of such a "discovery," or perhaps only the rediscovery of such a discovery, should entitle the individual making it to absolute control of the particular combination, and should further permit him to exact such profits as he sees fit.

Quite apart from the absurdity of the claim for proprietorship in each mixture is the assumption that because such a mixture is made by one certain individual or firm it must be invested with certain new or extraordinary properties and will, therefore, be superior to the same mixture when compounded by some other presumably less skillful persons. How far-reaching the further unrestricted progress of this species of proprietorship might become is indicated by the fact that at the present time the available proprietary mixtures number over 30,000 distinct preparations, and that the articles that are official in the Pharmacopeia of the United States alone would offer further possi-

bilities of untold thousands of similar "original" mixtures.

While it is reasonable to suppose that one manufacturer may possibly acquire a certain amount of skill in the combination of well-known ingredients, or may even be said to exercise greater care in the selection of the constituting materials, these assertions and claims are foreign to the question of proprietorship and may be conceded when such facts are actually demonstrated.

Among the factors that have contributed to a more reasonable view of proprietorship in medicinal compounds are the National Formulary and other books of its type. It is more particularly due to the general recognition that has been accorded the National Formulary, as an authoritative standard, that we are now able to differentiate between the reasonable announcements that are made by reputable manufacturers and the bold claims of absolute proprietorship, based on pretended priority of discovery, made by manufacturers of questionable nostrums.

That the use of well-established formulas, apart from those contained in the Pharmacopeia, is not a recent one is well illustrated by the natural sequence and the evolution of well-known formularies in this country.

The earliest of these, "Formulæ Selectæ, or a Collection of Prescriptions of Eminent Physicians," was published by R. Donaldson, New York, in 1818, two years before the first edition of the

Pharmacopeia of the United States was published in Boston.

From the preface of this early formulary it appears that its publisher fully appreciated the limitations and the needs of popular formulas and the contents of the book show that not a few of the problems that confronted the medical practitioners of that early date are still with us, though changed in character.

This, the earliest of the known American Formularies, was succeeded by a number of more or less similar publications that achieved considerable repute and popularity.

Among the more widely known of these early formularies it will suffice to enumerate Ellis' Medical Formulary, Beasley's Prescriptions, and Griffiths' Universal Formulary.

More than fifty years ago the American Pharmaceutical Association set for itself the task of compiling and promulgating a generally acceptable book of formulas. The first report of a committee on unofficial formulas was published in 1857, and the idea was periodically revived, from time to time, with but indifferent results.

After the publication of the Pharmacopeia of 1880 another concerted attempt was made by the American Pharmaceutical Association to compile an unofficial formulary. Under the able leadership of the late Dr. Charles Rice, of New York, as chairman, a committee presented "a preliminary draft of a national formulary" in 1886 and issued

the completed book in 1888. The second edition, under the editorship of C. Lewis Diehl, the present chairman of the Committee on National Formulary of the American Pharmaceutical Association, was published in 1896, and the third (1906) edition, or the second revision, has been accepted, with the Pharmacopeia, as a legal standard under the Food and Drugs Act.

The formulas that are contained in the 241 pages of this last edition may be divided into groups consisting of:

1. Formulas from former edition of the United States Pharmacopeia. These have been gathered together in the form of an appendix to the National Formulary and are thus readily available for reference.

2. Formulas official in foreign pharmacopeias which have been popularized to some extent in this country through medical literature, but not sufficiently used to warrant their being included in our national Pharmacopeia.

The many preparations of this type include well-known articles as Caffein Sodio-Salicylate, Ferrated Extract of Apples, Pectoral Species, Laxative Species, Spirit of Formic Acid and Ethereal Tincture of Ferric Chlorid, which are official in the German pharmacopeia.

3. Formulas introduced by prominent medical men or teachers that are either of comparatively recent origin or of restricted use.

This class of formulas is perhaps best illustrated

by the dermatologic pastes recommended by Lassar and Unna, for which a number of type formulas are included. Among others that come under this heading are Dobell's Solution, Loomis' Diarrhea Mixture and Squibb's Rhubarb Mixture.

4. Formulas representing present-day survivals of the old-time "patent medicines."

This class is represented by Turlington's Balsam, Dalby's Carminative, Bateman's Pectoral Drops, Godfrey's Cordial and others.

5. Formulas that closely resemble those of well-known nostrums, or so-called ethical proprietary remedies.

As noted before, this is a class about which there exists an honest difference of opinion. When we remember, however, that the most meritorious of these several nostrums represent very little that is original or novel (most of them having been appropriated from the prescriptions of well-known physicians), and that the claims that are made in connection with many of them are based largely on extravagance and deception, the propriety of using supposed imitations of any of them presents itself to us in quite a different light.

To illustrate how very little originality is represented by the average proprietary medicine and how, in not a few cases, the discoverer of the so-called new remedy has succeeded in simply disguising an old and well-known formula by imparting to it a new flavor, giving it some new color and conferring on it a new name, we refer to the fol-

lowing formulas contained in this late edition of the National Formulary:

The formula for "Alkaline Antiseptic" produces a preparation that is suggestive of the widely advertised proprietary "Glyco-Thymoline." From a therapeutic point of view this formula is evidently based on the old formula for "Compound Solution of Sodium Borate"—Dobell's Solution—the only evident difference being the substitution of the aromatic antiseptics for the "disagreeable" carbolic acid and imparting to the solution a characteristic color.

In the National Formulary the formula for "Chloral and Bromid Compound" is strongly suggestive of "Bromidia," but it also calls to mind the composition of the very much older and well-known English formulas for chloroform anodyne, chlor-anodyne and chlorodyne. The American "discoverer," it is true, has substituted a huge dose of hydrated chloral for a safer dose of chloroform and calls the resulting mixture a safe and harmless one, "the hypnotic par excellence." Aside from the manifest untruths that are to be found in the advertising matter put out by the concern manufacturing Bromidia, and the pharmaceutical "knack" in preparing it, there is nothing original or novel to be recorded in connection with it.

The Compound Digestive Elixir recalls the widely used Elixir of Lactopeptine, which, apart from its pretty red color and admittedly pleasing taste, has little to recommend it from a therapeutic point of view.

What is true of these preparations is also true of nearly all this class of mixtures that are now being exploited and sold as original preparations; they are original only in so far as they relate to the particular manufacturer and represent nothing really new or original.

The few examples enumerated above, therefore, serve to indicate that in place of presenting formulas for imitations of proprietary remedies the National Formulary really reflects how the demands of medical practice are met by improved pharmacy, to which the manufacturers of proprietaries have contributed but little.

Apart from the question of individual right in the formula or the composition of any particular preparation, is the fact that many nostrums marketed through physicians are so sold, advertised, prescribed and labeled as to induce self-medication by the laity, and many of them are advertised, at least indirectly, to the public. When we remember that not a few of these preparations represent dangerously potent drugs and that all of them are a menace to the public health, unless their use is intelligently directed, we must admit that as physicians we have been sadly remiss in our duty as guardians of the public health in even allowing (to say nothing of fostering) the present-day multiplicity of objectionable nostrums.

Even in connection with preparations that are otherwise unobjectionable there are serious abuses for which we are directly responsible. Not a few

of the manufacturers of medicinal preparations have assumed the rôle of scientific investigators and attempt at least to pose as such before us and before the public. In exploiting their wares, however, they commonly extol all of their virtues, but either minimize their disadvantages or, more frequently, omit all mention of adverse criticism. We would instantly discredit any scientific investigator detected in such deception, and if manufacturers continue to attempt to pose as scientific investigators we should, in justice to ourselves, demand the same standards in the exploitation of new remedies that we do in scientific research, and, above all, we should insist that we ourselves be not misled by garbled and unreliable reports of the wonderful cure-all properties of a new remedy.

As previously noted, it is our purpose in writing the following chapters to arouse and to foster a healthy spirit of skepticism regarding the claims made by manufacturers in connection with new, and in many respects unknown, remedies, and to cultivate, so far as we are able, a desire for authentic information bearing on the use of the time-tried and generally well-established remedies of the Pharmacopeia. To do this it will at times be necessary to present what may seem elementary and well-known facts. If we succeed in making many members of the medical profession more familiar with the drugs and preparations which are included in our national Pharmacopeia, we shall feel that we are well repaid for our efforts.

CHAPTER I.

GENERAL DISINFECTANTS.

The important subject of antisepsis embraces so many different agents that are used in such a variety of conditions that any convenient consideration of them according to their uses, or according to the principles that are involved, must necessarily be an arbitrary one. For our purpose we shall consider them under three heads: (1) General disinfectants and antiseptics; (2) local disinfectants and antiseptics, and (3) internal antiseptics. Some substances will require consideration under all three headings, but even this will be found preferable to giving, for example, all of the manifold uses of such an article as mercuric chlorid in one place.

Antiseptics were used long before the causes of fermentation or of putrefaction were known, and it would have been remarkable, indeed, had man failed to perceive the effect of those substances which are capable of inhibiting a process so commonly encountered. The Egyptians preserved the human body against the attacks of putrefactive organisms, without any evident knowledge of the character of the organisms causing decay, by means of balsams which contained such antiseptics as benzoic and cinnamic acids. The epoch-making discoveries of Pasteur, followed, as they were, by the favorable reports on the use of phenol, or carbolic

acid, by Lister, and the subsequent discovery that other substances possessing great antiseptic power were even less toxic to man, gave tremendous force to the pendulum, which was carried entirely too far by the efforts of well-meaning enthusiasts, and in its backward swing much unnecessary skepticism has been aroused.

The rapidly growing importance of preventive medicine has raised the subject of sanitation into one of prime interest, and the physician must at least inform himself on the general principles involved, including those of disinfection. In this connection attention may be called to the very general, but erroneous, impression in the lay mind that all deodorants are disinfectants—an error that often leads to dangerous dependence on substances which are useless for disinfection.

While the subject of general disinfection does not necessarily form a part of the physician's daily consideration, there are occasions when he is suddenly confronted with the necessity of directing such work, and on the thoroughness with which he does it will depend the safety of other members of the community. While there is no great difficulty in securing thorough disinfection, it is absolutely necessary that certain rules be rigidly complied with, and this can not be done without an exact knowledge of the object that is to be accomplished and of the means of the accomplishment. There is probably no condition where a little knowledge can prove to be more dangerous than in this very matter of disinfection, and we, therefore, have no apologies to offer for going into details on a subject

that may be considered commonplace or well understood.

That an ounce of prevention is better than a pound of cure is nowhere better demonstrated than in the matter of infectious diseases, and we may digress in order to consider the means of preventing certain communicable diseases.

Flies are very commonly the carriers of infection, and it is important that they should be destroyed, and, when possible, their breeding prevented. For the latter purpose all fresh manure should be promptly covered with milk of lime to prevent the hatching of eggs deposited in the manure. Stables should be screened when feasible. Milk infected in insanitary stables is one of the most prolific sources of disease, and the milk supply should be investigated whenever it seems probable that it may be the source of infection, particularly in scarlet and typhoid fevers, and in the diarrhea of infants. In the event that a sanitary condition is unattainable about the stable, prompt sterilization of the milk becomes necessary.

It is well known, through the work of Carlos Finlay, Reed and Carroll, Manson and others, that the mosquito is the carrier of the organisms concerned in the spread of malaria and yellow fever, and the destruction of those pests is, therefore, the first rational step toward the prevention of the spread of those diseases.

The complete extermination of the mosquito is not always easy, but precautionary measures will always lessen the danger from this source.

All bodies of still water, whether they be found in discarded tin cans or in ponds, may serve as the

breeding places of the mosquito, and they should, therefore, be drained or covered, in the mosquito season, with a thin film of oil at intervals of about two weeks. Patients suffering with malaria and yellow fever should be carefully protected by mosquito nets.

SUNLIGHT AND HEAT.

The best of all disinfectants is bright, direct sunlight, coming into immediate contact with the individual germs, not merely shining on one side of a thick garment or carpet, or on small masses of sputum, blood, pus or decaying meat, but shining on, and penetrating, each individual micro-organism. When this can be accomplished all germs—not all spores—are killed in a few hours. But sunlight is not dependable unless all of the necessary conditions can be rigidly complied with, as may be done with impervious flat surfaces (floors), or linen and other thin garments, both sides of which may be exposed to the direct rays of the sun. The disinfection of articles infected with the more virulent pathogenic organisms usually requires other, more directly active, means than that of sunlight, with the attendant danger of further dissemination, and chemic disinfectants or heat must then be employed.

The direct flame instantly destroys all forms of microscopic life. Dry air, heated to 160° C. (320° F.), kills all disease germs—but not all spores—in one hour; but wood will begin to char at 180° C. (356° F.) and even lower, so that dry hot air is not applicable as a certain means of disinfection in all cases. Simple drying kills bacteria; but

masses of sputum or other organic matter may preserve the organisms in the interior for an indefinite period, while spores are thus preserved for years.

Moist heat, water or air saturated with aqueous vapor, heated to 75° C. (167° F.), is rapidly fatal to most bacteria. Water containing typhoid bacilli is rendered much safer by heating even to this comparatively low temperature for ten minutes. Boiling water, on the other hand, will kill even spores in ten minutes or more if they are not protected in small masses. When such masses do exist 1 per cent. of soda or soap should be added to the water to dissolve the albuminous and other organic matter and at the same time to raise the boiling point slightly.

When metallic instruments are to be disinfected they may be boiled in water containing caustic soda, baking soda or borax, as those substances prevent rusting.

Moist steam, or air which is *supersaturated* with steam, is rapidly fatal to pathogenic organisms, but superheated dry steam is not so quickly fatal as is the moist at a much lower temperature. Pressure, moisture and increased temperature increase the effectiveness of all methods of disinfection. Moist steam penetrates better than dry air, but heavy fabrics may protect micro-organisms, and particularly spores, for a considerable time, and many articles, such as mattresses, can not be readily disinfected even in this way.

CHEMICAL DISINFECTANTS.

Formaldehyd was first obtained by Hoffmann in 1867, but its powerful antiseptic properties were observed by Loew and Fischer in 1886.

Formaldehyd, or formic aldehyd, is widely used as a disinfectant and sometimes as a food preservative. Since it has been detected in smoke, and even in the atmosphere, it follows that minute traces in food may be due to natural causes. The amount so absorbed can not be large, since one part of the gas renders from 15,000 to 50,000 parts of air irrespirable.

Anderson found great differences in the resistance of different bacteria to various strengths of formaldehyd; thus, the dysentery and white pus organisms resisted a 1 per cent. solution for two hours, while a 5 per cent. solution required forty-five minutes for the destruction of the tubercle bacillus in sputum.

These results, which are contrary to pretty generally conceived opinions, illustrate the importance of exact knowledge in the matter of disinfectants.

Formalin, or formaldehyd, does not actively corrode metallic instruments, nor does it injure fabrics. The vapor of the strong solution is very irritating to mucous surfaces; it combines with albumin and on this action depends its germicidal properties.

Tunicliffe and Rosenheim found that one part of formaldehyd to 5,000 of milk interfered with metabolism in weak children.

The disinfectant action of formaldehyd is increased by moist heat, as in the case of other agents.

From the experiments that were made in the Hygienic Laboratory of the Public Health and Marine-Hospital Service, it would appear that formaldehyd gas is not to be depended on, as a germicidal agent, at temperatures below 16° C. (60°

F.) or when the relative humidity of the atmosphere is below 65°.

While many of the available references on the use of formaldehyd gas as a disinfectant are contradictory, it has been satisfactorily demonstrated that the simple presence of dry formaldehyd gas in the atmosphere can not be taken as a criterion of efficiency and that more, rather than less, than the theoretic quantity of gas should always be used.

The use of solidified formaldehyd, more properly known as paraform, paraformaldehyd or trioxymethylen, a polymerized formic aldehyd, has been recommended as a source of formaldehyd gas. A. A. Young and others, however, have shown that paraform can be vaporized and condensed again as paraform, and it is highly probable that even under the most favorable conditions only a portion of the substance is converted into actively available formaldehyd gas.

Formic aldehyd, or formaldehyd, is now official as:

LIQUOR FORMALDEHYDI.—U. S. P.—Solution of Formaldehyd, containing about 37 per cent. by weight of formic aldehyd, an oxydation product of methyl alcohol. When rooms are to be disinfected this substance may be applied directly by washing or spraying, or it may be used in the form of vapor. For the latter purpose the windows and doors are tightly closed, paper being used to stop up the crevices, carpets should be removed or suspended and all drawers and closets opened and their contents so placed that the vapor will readily reach and penetrate every particle of fabric. Formaldehyd solution is then vaporized either in the room or through the keyhole with enough water to

saturate the air in the room. Considerable loss of formaldehyd occurs through decomposition during vaporization by heat, and it is, therefore, preferable to saturate sheets with the requisite quantity and suspend them in the room which is to be disinfected, or, better still, the solution may be sprayed from a suitable atomizer. The keyhole is then plugged and the room allowed to stand for from 12 to 24 hours. Novy advises 150 c.c. (5 fl. oz.) of the 40 per cent. solution, corresponding to about 165 c.c. (5½ fl. oz.) of the official, for each 1,000 cubic feet of air space. To increase the efficiency of the formaldehyd, 3 liters (3 quarts) of water are vaporized into each 1,000 cubic feet of space. If the atmosphere is damp, less water will be required, of course. Under ordinary conditions it is cheaper to destroy inexpensive mattresses than to disinfect them thoroughly. If they are of straw, destruction is readily accomplished by burning them out of doors.

Formaldehyd gas is much less effective in the disinfection of rooms containing furniture than it is for disinfecting bare walls and flat surfaces.

For the disinfection of rooms a mixture of 3 liters of formaldehyd and 3 kilos of unslaked lime with 9 liters of boiling water may be used for 50 cubic meters (1,800 cubic feet) of space. The lime is placed in a tub holding about 25 gallons, the water poured on it and the formaldehyd added, the room being closed for some hours.

The resulting milk of lime may be used afterwards for the disinfection of feces and for other purposes enumerated later.

Another method of generation that is frequently recommended consists in placing from six to eight

ounces of potassium permanganate in a capacious tinned iron container and pouring on it 16 fluid-ounces of the official solution of formaldehyd. The reaction that follows is a complicated one, but takes place with great violence and several serious fires have been reported as the direct result of the spontaneous combustion of the evolved gas. To obviate this, it has been recommended to guard against the presence of organic matter and to place the generating container in a larger vessel, or tin tub, containing water.

The fumes of ammonia have a strong affinity for formaldehyd gas and the last traces of the latter may be readily absorbed by exposing a small quantity of ammonia in the room after it has been fumigated.

CALX.—U. S. P.—Lime, calcium oxid, constitutes an inexpensive and very useful disinfectant that has a number of widely varying uses. Infected urine, vomit and feces may be thoroughly disinfected by being received into a vessel that contains freshly prepared milk of lime. It is essential that this be freshly prepared, as calcium hydrate rapidly absorbs carbon dioxid from the air and is thereby changed into the inactive calcium carbonate. Milk of lime may be prepared by putting a few pounds of lime into an iron pot and adding about half as much water; the lime rapidly falls into a dry powder with the evolution of heat; to this powder add three times as much water and stir well. The resulting mixture will keep for several days without deteriorating sufficiently to be inert. There are, of course, several precautions to be observed: The lime must be recently calcined, or fresh, and the person who slakes

it should be careful to avoid the irritant dust which arises during the process; then, too, the heat generated may be sufficiently high to char wood or to set fire to readily combustible materials. For disinfecting feces or other substances they should be thoroughly stirred with an equal quantity of the milk of lime, or, better still, with twice the quantity, the mixture being allowed to stand for two hours.

Milk of lime is also useful for disinfecting floors, cellars, cesspools after draining, and even walls when they are not subject to injury. It must always be remembered that this whitewash rapidly absorbs carbon dioxid and thus becomes inert, hence the mixture is an efficient disinfectant, but it is not useful as an antiseptic.

Unslaked lime is a cheap and very efficient means of destroying animal matter and is also useful for absorbing moisture in damp cellars. As noted before, certain precautions are always to be taken in connection with this really active chemical substance. Cesspools are difficult to disinfect. Large quantities of milk of lime are effective, but the contents must be thoroughly mixed with the disinfectant, whatever its nature.

HYDRARGYRI CHLORIDUM CORROSIVUM.—U. S. P.—Corrosive Mercuric Chlorid, bichlorid of mercury, mercuric chlorid, or, as it is most commonly called, corrosive sublimate, will be considered more extensively in connection with local antiseptics. It has, however, a number of very important uses in connection with disinfectants.

Corpses of persons dead of an infectious disease should be immediately wrapped in cloths saturated

with a 1 to 1,000 solution of mercuric chlorid. The addition of 20 per cent. of glycerin to the solution of mercuric chlorid will prevent the rapid evaporation of the water, which leaves the mercuric chlorid as a dry powder in the cloth. Water which has been used to bathe a person suffering from an infectious disease, such as typhoid fever, should be disinfected by heating to near the boiling point or by the addition of a liberal quantity of milk of lime or a much smaller quantity of mercuric chlorid. If the bathtub is of metal, the latter chemical should not be used, but phenol or cresol may be substituted.

FERRI SULPHAS.—U. S. P.—Ferrous Sulphate, preferably the impure or crude article, commonly called copperas, is an excellent deodorizer for animal excretions, the iron uniting with the albumin and the acid with the ammonia; it is not a very active disinfectant.

CUPRI SULPHAS.—U. S. P.—Copper Sulphate, or blue vitriol, may be similarly used, but it is much more expensive and possesses no marked advantages over copperas as a deodorizer.

SULPHUR SUBLIMATUM.—U. S. P.—Sublimed Sulphur, or flowers of sulphur, is frequently burned as a disinfectant, in rooms which contain nothing which can be injured by the corrosive action of the resulting sulphurous oxid. It is not so frequently used now that formaldehyd affords a more satisfactory means of disinfection, but it is cheaper and may be used to advantage in cellars and in empty rooms, that can be thoroughly sealed. Hoppe-Seyler recommends that 15 gm. (½ oz.) be burned for every cubic meter (cubic yard) of

space. This would be equivalent to about 450 gm. (15 oz.) for 1,000 cubic feet. Rooms should be left tightly closed for from twenty-four to forty-eight hours, then the remaining fumes may be readily absorbed by sprinkling ammonia in the room. As with formaldehyd disinfection, the vapor must come into actual contact with the micro-organisms and the atmosphere should contain moisture. This latter requirement is usually met by burning the sulphur in a double vessel, the outer one containing water.

The gas that is generated by the burning of sulphur is very poisonous to man, due to its local corrosive action. Spasmodic closure of the glottis may occur, causing death. Sulphurous oxid, the substance that is thus generated, remains free in mixtures of organic matter longer than free chlorin, hence it is a more effective bactericide.

Owing to the poisonous nature of this gas, for all forms of animal life, it has been widely used to destroy vermin in infected rooms. It is much more efficient for this purpose than formaldehyd, though not so satisfactory as hydrocyanic acid gas; the latter; however, is extremely poisonous and must be handled with great caution.

CALX CHLORINATA.—U. S. P.—Chlorinated Lime, popularly, though improperly, called chlorid of lime, is a ready source of chlorin and is a very convenient and inexpensive disinfectant suitable for many of the purposes for which sulphurous oxid might be used. Chlorin, like sulphurous oxid, is very corrosive, attacking metals, and bleaching and destroying fabrics. Chlorinated lime is useful for sprinkling about urinals, damp cellars, out-

houses, stables and drains. It deteriorates rapidly on exposure to the air and only tightly sealed packages from reliable firms should be used.

Empty rooms may be disinfected with chlorinated lime when the walls can not be injured by the liberated chlorin. For this purpose 3 pounds of the chlorinated lime are used for each 1,000 cubic feet of space. It is placed in an earthen vessel, and a considerable amount of mineral acid is added, the room being left tightly closed for some hours. The gas is very poisonous and should not be inhaled.

The various solutions of chlorids that are sold at fancy prices are usually feeble and are in nowise superior to a readily made mixture of a quarter of a pound of chlorinated lime with half a gallon of water. The admixture of an acid at the time of using causes the rapid liberation of chlorin and increases the disinfectant action.

LIQUOR SODÆ CHLORINATÆ.—U. S. P.—Solution of Chlorinated Soda, the so-called Labarraque's solution, is but another form of a chlorin compound. It has the one advantage of being free from insoluble caustic material.[1]

PHENOL.—U. S. P.—Phenol, the Acidum Car-

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1. Where an inodorous deodorant is required it will be found that the Liquor Zinci et Alumini Compositus of the National Formulary will give better and more uniform satisfaction than proprietary articles of the same type. It is made as follows:

℞.	Zinci sulphatis Alumini sulphatis, āā	ʒxxvii	100
	Betanaphthol	gr. v	3
	Olei thymi	gr. xv	1
	Aquæ, q. s. ad	Oi	500

The salts are dissolved with the aid of heat and the volatile substances added to the solution.

Still another preparation of the same type is the Liquor Zinci et Ferri Compositus—N. F.

bolicum of the U. S. P. 1890, is much more expensive than, and not nearly so efficient as a disinfectant as:

CRESOL.—U. S. P.—Cresol has been included in place of the formerly official crude carbolic acid. It is a mixture of the three isomeric cresols found in coal tar, and is a useful and highly efficient disinfectant and antiseptic.

LIQUOR CRESOLIS COMPOSITUS.—U. S. P.—Compound Solution of Cresol consists of a mixture of equal parts of soap and cresol. When properly made this mixture is an admirable substitute for any one of the numerous soluble or semi-soluble proprietary preparations containing cresol; such as creolin, cresolin, lysol, lysitol and a host of others too numerous to mention.

Compound solution of cresol is practically identical with the Liquor Cresoli Saponatus of the German Pharmacopeia; it is miscible in all proportions with water, and, as noted before, is a reliable and readily available disinfectant.

One part of the compound solution of cresol added to twenty parts of very warm water is useful for the sterilization of surgical instruments, and a slightly weaker solution, made by adding one part to thirty of warm water, affords an excellent disinfectant for the hands.

POTASSI PERMANGANAS.—U. S. P.—Potassium Permanganate attacks all forms of organic matter and is generally useful for the destruction of foul odors, but is not very useful as a disinfectant. It will be considered later at greater length.

The strong mineral acids are destructive to bac-

teria, but their application as disinfectants is necessarily very limited.

As noted before, mercuric chlorid is to be classed with the most powerful of all disinfectants in general use, one part in 10,000 being fatal to spores. Like all other chemical disinfectants, its activity is increased by heat. It precipitates albumin and its efficiency is, therefore, materially lessened by the presence of any appreciable amount of such organic material; this disadvantage of mercuric chlorid may be obviated in part by the addition of an equal amount of sodium or ammonium chlorid (or a small amount of hydrochloric acid), the tablets found on the market for preparing the solutions always containing the requisite quantity of one of those salts. As it attacks metals, it is not suited for the disinfection of instruments or metallic vessels. One part of mercuric chlorid in 50,000 parts of water has been demonstrated to possess decidedly antiseptic properties. Its comparative non-volatility, its property of attacking metals and of combining with albumin, and its extreme toxicity limit its field of application, but it remains by far the cheapest antiseptic we have for general use.

Copper sulphate shares with copperas (crude ferrous sulphate) the power of deodorizing decomposing organic matter, though it is but little used for this purpose. It has recently been claimed that the merest trace of copper sulphate, or of copper, in water readily destroys the bacillus of typhoid fever, or at least completely inhibits its growth; even though the copper is present in quantities too small to interfere with the use of the water for

drinking. The results of different investigators are not uniform, however, and some maintain that the antiseptic power of copper and its salts has been greatly overestimated. The soluble salts of zinc, particularly the chlorid, have also been used for disinfecting purposes, but as they share with copper the disadvantage of being comparatively expensive, without any accompanying material advantages, a more detailed consideration of these substances may be omitted in this connection.[2]

CLINICAL THERMOMETERS AND HYPODERMIC SYRINGES.

The disinfection or sterilization of clinical thermometers and of hypodermic syringes and needles deserves especial mention. With the present comparatively low price of clinical thermometers there is little or no excuse for not having an individual thermometer for each patient ill with an infectious or a contagious disease or a continued fever. But, even this precaution, desirable as it certainly is, does not obviate the necessity for disinfecting or sterilizing the thermometer. The necessary disinfection may be effected in any one of a number

2. The following quotation, taken from Wood's "Therapeutics," page 823, contains suggestions that are of interest in this connection. "There are not many affairs in life in which the public has been so super-abundantly fleeced as in the matter of disinfection. A most extraordinary part of this swindling is the ease with which distinguished members of the medical profession have given certificates of efficiency and value to comparatively inert and extraordinarily expensive proprietary compounds. Oddly enough, the cat that has drawn the chestnuts out of the fire for avaricious manufacturers has not even had the sense to smell the odor of its own paws when burning." It is evident that Dr. Wood knew less of the resources and the wiles of nostrum makers, and their shrewdness in duping physicians, than he supposed, else he would not think it extraordinary that so many have been deceived.

of ways; the thermometer may be dipped for a few minutes in strong phenol, the solution of cresol, or in the, now official, solution of formaldehyd, after which it is thoroughly rinsed in water. Where an individual thermometer is provided it may be sterilized by keeping the bulb immersed in 75 per cent. alcohol, a saturated solution of boric acid, the official liquor antisepticus, or in a mixture of equal parts of antiseptic solution and of solution of hydrogen dioxid. It must appear even to the least careful that the disinfection of clinical thermometers is a precaution so important that it should never be neglected.

The hypodermic syringe and needle should be disinfected with strong phenol or cresol solutions, solution of formaldehyd or by repeated washing with very hot water as a purely routine procedure. When a syringe and needle are known to be infected the disinfection should be as thorough as that of other surgical instruments.

Solutions intended for hypodermic injection can be sterilized by boiling, when this does not cause decomposition. With the now widely used hypodermic tablets it is preferable to boil the necessary quantity of water, or, better, distilled water, for a minute or two, then add the tablet, avoiding all unnecessary handling, and warm sufficiently to insure thorough solution. Cocain, being readily decomposed, can not be boiled, but the solution may be sterilized by heating to about 80° C. (176° F.) for thirty minutes on two successive days. It is usually preferable, however, to use freshly prepared solutions that have been made in a sterile bottle with recently boiled and sterile distilled

water. Eucain and stovain solutions may be boiled, but these substances themselves are not entirely free from objections.

Under the subject of internal antiseptics we shall have occasion to mention the disadvantages of sterilized milk, but here we may call attention to the widespread use of formaldehyd, salicylic and boric acids, borax and other chemical antiseptics for the preservation of foods. While we are not certain that minute quantities of many of these chemical antiseptics are in themselves injurious, we have ample authority for the opinion that their continued use in appreciable quantities is by no means beneficial. Schmiedeberg regards the constant use of even small quantities of salicylic acid, for a continued period, as unwise in the present state of our knowledge, and Sollmann says that the use of formaldehyd can not be too strongly condemned, because of the specific irritation of the mucous membranes which it causes.

Liebreich has written a number of treatises on the use of boron compounds as food preservatives, but The Prussian Scientific Deputation on Medical Conditions gives a written opinion at the request of the Berlin police, in which the conclusions of Liebreich are rejected, and these preparations are pronounced injurious to the human organism even when taken in small quantities.

The whole subject of food preservatives, from its vital importance, is one in which the physician should, and indeed must, be actively interested, but it is entirely too extensive to be discussed at length here.

The subject of preservatives is also of interest

in connection with medicines and medicinal preparations. The antiseptic action of alcohol, glycerin, sugar and of volatile oils is well known and generally recognized, and, while not of sufficient importance to be considered in connection with general disinfection, these substances are widely used as preservatives not alone for medicinal preparations and foods, but also for other substances. The use, or abuse, of preservatives in connection with medicinal preparations, particularly in connection with proprietary remedies, is a matter that is deserving of more attention than is now being accorded it; as the presence of preservatives undoubtedly influences the physiologic action of other ingredients.

CHAPTER II.

LOCAL DISINFECTANTS AND ANTISEPTICS.

Lister's use of local antiseptics in surgery is usually spoken of as a discovery, but, without detracting in any way from the credit due to Lister, it should be referred to more correctly as a practical application of previous discoveries.

Reichenbach, in 1832, obtained a substance from wood tar which he named creosote. Finding later that it consisted of phenol and phenol ethers, and also finding these same substances in smoke, he concluded, and later conclusively proved, that to them is due the meat preserving activity of smoke.

Runge, in 1834, found that the phenol which he obtained from coal tar also possessed the power of preventing putrefaction. Tar and a number of products of a similar nature were long ago recommended and widely used for foul smelling ulcers, but the fact remains that to Lister is universally, and very properly, accorded the distinction of having placed antisepsis in surgery on a sure basis. Since the early days of antisepsis there have been many improvements, and we now know that the most perfect cleanliness, or asepsis, that is attainable is much to be preferred even to the most elaborate antisepsis.

It is, of course, entirely beyond the scope of this treatise to consider the details of major surgery, but the principles of antisepsis which obtain in this branch are equally applicable to minor

operations, and their disregard by many, who are not surgeons, is the best justification for their present brief consideration. The necessity for scrupulous cleanliness is seen in such a common, but admittedly important, procedure as vaccination. The careful physician will perform even this simple operation under aseptic conditions, thereby saving himself much annoyance in case of accident.

The first, and really the most important, duty of the physician with regard to infections is to see that he does not carry them to other patients. There can be no doubt that physicians have played no small part in the spread of infectious diseases, particularly in the past, but fortunately, with the better understanding of the subject, this occurs now less frequently than it did formerly.

The disinfection of clothing and of instruments belongs to the subject of general disinfection, that of the hands and person to local disinfection.

The cleansing of the hands, as it is done in a number of American hospitals, is about as follows: "Trim and clean the nails, wash the hands and forearms for five minutes in very warm, sterile water, using soft soap or a liquid soap[1] and

1. An efficient and satisfactory liquid soap can be prepared by any pharmacist from the following formula:

Sodium hydrate	40 Gm.
Potassium hydrate	40 Gm.
Cottonseed oil	500 Cc.
Alcohol	250 Cc.
Distilled water, a sufficient quantity to make	2500 Cc.

In a suitable container, preferably a glass-stoppered bottle, dissolve the potassium hydrate and the sodium hydrate in 250 Cc. of distilled water, add the alcohol, and then add the cottonseed oil in three or four portions, shaking vigorously after each addition. Continue to agitate the mixture occasionally until saponification has been completed. Then add the remaining portion of distilled water and mix.

scrubbing them energetically with a brush or a gauze pad, cleansing the nails again during this part of the process. Rinse the hands for three minutes in 75 per cent. alcohol, to remove soap and to aid in sterilization; then in 1 to 1,000 solution of mercuric chlorid, or in a solution of 1 to 2,000 mercuric chlorid with 1 to 40 phenol, and finally rinse in sterile warm water." This may be somewhat more elaborate than is necessary in most cases of minor surgery, but even here it is well to err on the safe side.

For the disinfection of the whole body a full bath in warm water with the liberal and judicious use of soap is sufficient, and the clothes may undergo disinfection separately at the same time. This procedure is so simple that the physician can not escape blame should he carry infection from one patient to another through the omission of necessary precautions.

When minor surgical operations are to be performed it is always well to thoroughly disinfect the surface at and around the prospective seat of operation. For this purpose the procedure given for cleansing the hands of the surgeon is sufficient, though in some cases it may be found necessary to supplement the soap and water with oil of turpentine.

Wounds and ulcers require disinfection to destroy those bacteria which can be reached, and antiseptic dressings to prevent the development of colonies from those which escape destruction or which may afterward reach the spot.

The compound solution of iodin has been used to disinfect cysts in which putrefactive processes

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are going on, but this process is extremely painful and sometimes dangerous. It is not recommended.

AQUA HYDROGENII DIOXIDI.[2]—U. S. P.—Solution of Hydrogen Dioxid, or, as it is frequently called, Solution of Hydrogen Peroxid, is useful for decomposing pus, in which bacteria are protected from the action of other disinfectants. It thus secures the rapid cleansing of freely exposed pus cavities or ulcers, and at the same time it acts powerfully on bacteria, though they are not all destroyed so long as any pus remains. The official solution is equal, in disinfectant power, to a 1 to 1,000 solution of mercuric chlorid. The action on pus of hydrogen dioxid is so extremely rapid that it frequently detaches small masses which may escape decomposition.

The use of this solution is not unattended with risks, particularly in sinuses or deep, partially closed, wounds. Mucous membranes decompose hydrogen dioxid rapidly, and the skin slowly, with the liberation of nascent oxygen. It is not certain whether the bactericidal property is due to the liberation of oxygen alone, or whether the preparation possesses a special influence on the micro-organisms. The decomposition whereby the oxygen is liberated is supposed to depend on a ferment, catalase, which is widely distributed, and, as the preparation loses its bactericidal powers, once the oxygen has been liberated, it is, of course, useless

2. It is commonly, but erroneously, believed that the amount of free gas confined in the bottle is an index of the value of the solution of hydrogen peroxid. It is, in fact, an index of the amount of decomposition that has occurred. Many manufacturers of hydrogen dioxid now use acetanilid as a preservative. When such a solution develops an odor resembling nitrobenzol it should be discarded.

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as an antiseptic, though extremely useful as a disinfectant. Hydrogen dioxid has an especial reputation in the treatment of sore throat and even diphtheria, for which it is used as a spray, or as a gargle, with entire safety. It attacks metals readily, and only rubber or glass should be used in connection with it. Diluted with an equal amount of water, it is an excellent wash for the mouth and throat, but not infrequently it contains a little acid, and the mouth should be rinsed after its use.[3]

After the disinfection of ulcers and wounds an antiseptic dressing is applied. Cotton, gauze and lint impregnated with various antiseptics are found on the market. Only the active substances that are used in this connection will be discussed, as the application of dressings belongs to surgery.

IODOFORMUM.—U. S. P.—Iodoform, Tri-iodomethane is usually obtained by the action of iodin on alcohol, in the presence of an alkali or an alkaline carbonate. Iodoform was discovered by Sérullas, in 1822, but was not used in medicine until some time after 1837. Despite its disagreeable penetrating odor, iodoform continues to hold first place among local antiseptics, used for the dressing of wounds. At first it was supposed to share with chloroform (from which it differs chemically only in containing iodin in place of the chlorin) a strong antiseptic action, but in the case of iodoform this has been found to be but slight; it is, however, materially increased by the slow

3. An agreeable, and at the same time efficient, mouth wash is obtained by mixing equal parts of aqua hydrogenii dioxidi, liquor antisepticus (U. S. P.) and a saturated solution of potassium chlorate.

liberation of iodin. When its local use as a dressing is long continued, enough of it may be absorbed to produce poisoning, which does not, however, result in typical narcosis, such as chloroform produces, but gives rise to disturbances of cerebration, headache, delirium and other symptoms. These are due to the iodoform molecule; but exanthemata, which are sometimes severe, are usually attributed to the liberated iodin, which, when liberated. is thought to circulate in the blood as an alkaline iodid or in combination with albumin. Hematuria, albuminuria and urinary casts may also result from its absorption, and many attempts have been made to find a substitute for iodoform without its poisonous effects.

Some surgeons deny that iodoform exerts any direct antiseptic power, and attribute the benefits from its use to its limitation of the secretion on which the bacteria would otherwise develop. Binz observed that iodoform lessened the emigration of leucocytes, and it is said to be particularly useful in local affections with free secretions.

When iodoform is intended for use as a dusting powder, its odor may be rendered very much less disagreeable by incorporating with it from 1 to 4 per cent. of cumarin. The following has been used to some extent:

℞.	Iodoformi	ʒv	20
	Cumarini	gr. xv	1
	Acidi borici q. s. ad	ʒxiii	50

Misce bene.

Sig.: To be used as a dusting powder.

Pulvis Iodoformi Compositus (N. F.), containing iodoform 20, boric acid 30, naphthalin 47, and oil of bergamot 3 parts, also constitutes a use-

ful and comparatively unobjectionable antiseptic dusting powder.

Where iodoform is to be used in the form of an ointment the addition of from 5 to 10 per cent. of balsam of Peru, or of 2 per cent. of oil of anise has been found to be advantageous. The addition of oil of anise, in somewhat larger quantities, has also been recommended for iodoform gauze, particularly when the gauze is to be used in appreciable quantities or for any continued length of time.

If the antiseptic action of iodoform is due to the liberated iodin, then necessarily many of the proposed substitutes must be practically devoid of antiseptic power, since the iodin is too firmly bound to be liberated by the tissues.

IODOLUM.—U. S. P.—Iodol, designated chemically as tetra-iodopyrrol, is one of the recent additions to the Pharmacopeia. The iodin in this case is so firmly bound that the substance has been recommended as being comparatively non-toxic, but iodin is liberated in the body, being excreted as iodid. Other preparations, such as nosophen, losophan and europhen, depend largely for their antiseptic action on the cresol or the phenol compounds united to the iodin. Loretin and vioform are combinations of iodin and quinolin, and there is no reason to suppose that they have any advantage over the other preparations just mentioned.

THYMOLIS IODIDUM.—U. S. P.—Thymol Iodid, much better known by the formerly trademarked name "Aristol," is a condensation product of two molecules of thymol with two atoms of iodin, and more properly, therefore, should be designated by

its true chemical title, dithymol di-iodid. This preparation, which really belongs to the phenol group of iodin compounds, has met with a better reception than many of the other iodoform substitutes. It is probable, now that the patents have expired on aristol and the substance is available at much more reasonable prices, that its popularity and use will be extended still further. This, however, is problematic. Schmiedeberg specifically states that aristol, losophan, sozoiodol, picrol, loretin and antiseptol, all of which contain iodin, are not more actively antiseptic than are the corresponding iodin free compounds, while the latter are, of course, much less expensive. Since the number of possible combinations of this type is practically unlimited, we will do well to exercise circumspection in accepting those which appear from time to time.

PHENOL.—A sharp distinction is to be drawn between the anesthetic and antiseptic uses of phenol. Solutions of phenol in oil, or mixtures with fats, are excellent anesthetics when brought in contact with painful surfaces or wounds, but they possess very little antiseptic action, because phenol is more soluble in fats and oils than in water or weak saline solutions, hence it does not leave the oil to penetrate the bodies of bacteria, without doing which it does not injure them.

Practically the same holds true of its affinity for alcohol, and it is for this reason that alcohol is such an excellent antidote for carbolic acid, externally as well as internally. The absorption of phenol is followed by its appearance in the urine,

which usually becomes dark-greenish or nearly black in color.

The toxicology of phenol deserves a passing notice. Despite the well-known fact that it occasions great pain when swallowed, it was selected as the agent of destruction by more than one-third of all those who committed suicide by poison in England for a number of years. It is probable that poisoning by it is equally frequent in this country.

Sodium sulphate is commonly stated to be the proper antidote, though experiments made on animals have never demonstrated that it possessed any very decided value, and Sollmann and Brown have recently shown that it has practically no effect on the course of the poisoning.

Kobert relates that each of two children swallowed a teaspoonful of liquefied phenol; ten minutes afterward their stomachs were washed out and their lives were thus saved.

PHENOL.—U. S. P.—(Acidum Carbolicum U. S. P., 1890) is hydroxybenzene; it may be obtained from coal tar by fractional distillation and subsequent purification, or it may be made synthetically. In its pure state it occurs as colorless, needle-shaped crystals, or as a white crystalline mass.

PHENOL LIQUEFACTUM.—U. S. P.—Liquefied Phenol, Liquid Carbolic Acid, contains from 85 to 89 per cent. of absolute phenol, and is the form in which phenol is usually seen and used. When first prepared this solution is colorless, but it frequently develops a reddish tint on keeping.

Phenol is now used as an antiseptic dressing for wounds very much less frequently than it was some years ago, because of the danger of poison due to

absorption. It may be applied in the form of a 2 per cent. solution in water; stronger solutions are used, but many cases of gangrene have followed the use of even dilute solutions on the extremities, particularly the hands, for a continued length of time.

CRESOL.—U. S. P.—and its more desirable form:

LIQUOR CRESOLIS COMPOSITUS.—U. S. P.—Compound Solution of Cresol is well known and has been extensively used, particularly in the form of one or the other of the numerous proprietary preparations, as a local disinfectant and also as an antiseptic. The saponaceous properties of this particular preparation make it very useful in a variety of instances in which a detergent action is to be attained in addition to the disinfection.

THYMOL.—U. S. P.—This is a phenol occurring in the volatile oil of *Thymus vulgaris* and in some other volatile oils. It possesses strong antiseptic properties, but its comparative insolubility in water, 1 in 1100, has interfered materially with its extended use. Thymol iodid, the only official combination of thymol, has been referred to in connection with iodoform substitutes.

An ideal disinfectant, or antiseptic dressing for wounds, should act not strongly on the living protoplasm, should be slowly absorbed, and should affect the central nervous system but slightly after absorption. Phenol has the disadvantage of being rapidly absorbed and of profoundly affecting the central nervous system. Thymol, being but slightly soluble in water, but volatile at ordinary temperatures, is slowly absorbed, and, as its excretion keeps pace with its absorption, there is little dan-

ger that it will exert a poisonous action when used locally.

The practice of dermatology involves a special knowledge of antisepsis, and the subject can be given only general consideration at this time, so that we must content ourselves with little more than a simple enumeration of some of the official substances that are used, merely suggesting the number and variety of the available materials.

RESORCINOL.—U. S. P.—(Resorcinum U. S. P. 1890), a diatomic phenol that is usually referred to by its popular name, resorcin, was at one time extensively used in dermatologic practice, but is now seldom employed except for scalp diseases and sometimes internally.

PYROGALLOL.—U. S. P.—This is better known as pyrogallic acid and is a triatomic phenol, sometimes used in dermatologic practice.

ACIDUM SALICYLICUM.—U. S. P.—Salicylic Acid has been used to some extent as a local antiseptic, particularly in the form of dusting powders, diluted with talcum, zinc oxid or boric acid. Salicylic acid is used extensively in dermatologic practice, particularly in the form of ointment. It is only slightly soluble (1/310) in water.

PIX LIQUIDA.—U. S. P.—Tar, a product obtained by the destructive distillation of the wood of one of several species of *Pinus,* has been widely used in the treatment of skin diseases, usually in the form of an ointment.

UNGUENTUM PICIS LIQUIDÆ.—U. S. P.—Tar Ointment contains 50 per cent. of tar.

OLEUM CADINUM.—U. S. P.—Oil of Cade, or oil of juniper tar, is a product of the dry distilla-

tion of *Juniperus Oxycedrus* and is closely allied to tar, being used in the same way.

BALSAMUM PERUVIANUM.—U. S. P.—Balsam of Peru will be referred to again under expectorants. Its antiseptic properties are probably due to the benzoic and cinnamic acids which it contains. It is used in dermatology, either in ointment or in collodion.

NAPHTHALENUM.—U. S. P.—Naphthalene or naphtalin and

BETANAPHTHOL.—U. S. P.—Naphtol, are used in dermatologic practice, though the former, at least, has practically fallen into disuse for medicinal purposes.

Among other substances having antiseptic properties, used locally, we have:

SULPHUR PRECIPITATUM.—U. S. P.—Precipitated Sulphur. This and the other official forms of sulphur will be mentioned also in connection with cathartics. Sulphur constitutes a most important agent in the treatment of a number of skin diseases. It is applied either in the form of lotions or of ointments. For the former, precipitated sulphur is usually preferred, while in ointments either

SULPHUR SUBLIMATUM.—U. S. P.—Sublimed Sulphur, or

SULPHUR LOTUM.—U. S. P.—Washed Sulphur is used. In the official

UNGUENTUM SULPHURIS.—U. S. P.—Sulphur Ointment, 15 per cent. of washed sulphur is directed to be used. This ointment is now only half the strength of that formerly official and is, there-

fore, better suited as a mildly stimulating antiseptic application.

SODII THIOSULPHAS.—U. S. P.—Sodium Thiosulphate, better known as sodium hyposulphite, is another useful antiseptic that is now little used medicinally, except in dermatology. It is freely soluble in water and is usually prescribed in the form of a lotion. It is said to be particularly useful in the destruction of parasitic fungi which infest the skin.

GLYCERINUM.—U. S. P.—Glycerin is not alone useful as a mild antiseptic, but is also extensively used as a vehicle for many other substances in the treatment of skin lesions.

GLYCERITUM AMYLI.—U. S. P.—Glycerite of Starch is a preparation that was introduced many years ago to serve as an ointment base in cases in which lard or fat might prove objectionable. It was formerly used as a poultice in erythema, erysipelas, furuncle and various other local inflammations of the skin, and may be considered as the prototype of the almost innumerable glycerin clay mixtures now offered.

MERCURIALS.

HYDRARGYRI IODIDUM RUBRUM.—U. S. P.—Red Mercuric Iodid or biniodid of mercury is the most active of all the official germicides and antiseptics. It is comparatively expensive, however, and is only slightly soluble in water.

HYDRARGYRI CHLORIDUM CORROSIVUM.—U. S. P. Corrosive Sublimate is by far the most popular and most generally used of all local chemical disinfect-

ants and antiseptics. It is extremely poisonous and many fatalities have occurred from its use, even in the vagina and in the washing of wounds.

Mercuric chlorid is slowly but completely soluble in 13 parts of water and in 3 parts of alcohol. The solubility of this substance in water is much facilitated by the presence of other soluble chlorids. This fact has been utilized in the preparation of the commercial tablets of mercuric chlorid that are sold for making antiseptic solutions. These tablets usually contain about 0.5 gm. (7.5 grains) each of mercuric chlorid and ammonium chlorid, the sal alembroth of the alchemists, which, when dissolved in 500 c.c. (1 pint) of water make a solution of 1 to 1,000. This solution is useful for the disinfection of the hands, for walls and floors and for many fabrics that are not injured by water. Gauze impregnated with a solution of mercuric chlorid is often placed over small or closed wounds to prevent the access of bacteria. It is widely used as an antiseptic and disinfectant, but it is extremely caustic and can not be applied to mucous membranes and to open wounds except in very dilute solutions, for fear of absorption.

Mercuric chlorid attacks metals and must be avoided, therefore, with metallic instruments. It is a very popular insecticide and a number of the mercurials are used as parasiticides, notably for pediculi. For this purpose, however, the various ointments of mercury are more frequently used.

UNGUENTUM HYDRARGYRI.—U. S. P.—Mercurial Ointment contains 50 per cent. of mercury.

UNGUENTUM HYDRARGYRI DILUTUM.—U. S. P. —Blue Ointment, a new addition to the Pharmaco-

peia, contains 33 per cent. of mercury and conforms more closely to the proposed international standard for mercurial ointment. Another ointment that is sometimes used as a parasiticide is

UNGUENTUM HYDRARGYRI OXIDI RUBRI.—U. S. P.—Ointment of Red Mercuric Oxid, or red precipitate ointment, containing 10 per cent. of red mercuric oxid.

ANTISEPSIS OF THE MUCOUS MEMBRANES.

The antisepsis of the mouth is important, not only because of the infectious diseases pertaining to it, but also because of the excellent opportunity that is afforded to micro-organisms to multiply there in enormous numbers on the particles of food in the cavities of teeth or wedged between them. That this is true is shown by the putrid smell acquired by particles of meat which remain but an hour or so in the mouth. The extent to which bacteria may increase may be inferred from the calculation, given by Novy, that 30,000,000,000 contain less than one-sixth of a milligram (1/400 grain) of organic matter.

The main factor in securing antisepsis of the mouth is cleanliness. If the teeth are carefully cleansed and all organic matter removed, the bacteria have less on which to thrive, and mild antiseptics then fully suffice to keep the number within bounds.

LIQUOR ANTISEPTICUS.—U. S. P.—Antiseptic Solution is a new addition to the Pharmacopeia, containing 2 per cent. of boric acid with aromatic antiseptic volatile oils. It is designed to be used

as a mildly antiseptic lotion or wash,[4] as are numerous similar proprietary preparations.

It must be remembered that the name of this official antiseptic solution is a misnomer in effect, if not in fact, since it possesses at most but very weakly antiseptic properties, being a detergent rather than an antiseptic.

Antiseptic Solution is also useful as a gargle, preferably diluted with an equal quantity of water. The use of solution of hydrogen dioxid as a spray or gargle, as well as its use in connection with the official antiseptic solution, has been mentioned.

POTASSI CHLORAS.—U. S. P.—Potassium Chlorate, while not a particularly active antiseptic, has long been favorably known to be a desirable addition to gargles and mouth washes. It is soluble in 16 parts of cold water and is generally used in saturated solution, from which traces of chloric acid may possibly be liberated. Alum and boric acid are also useful as gargles.

Free chlorin is an effective disinfectant and it may be utilized in the form of a gargle, being liberated by the action of hydrochloric acid on po-

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4. The official antiseptic solution is slightly acid. When an alkaline antiseptic mouth wash is desired it will be well to use the "Alkaline Antiseptic Solution" of the National Formularly. Either one of these preparations can be prepared readily by any trained pharmacist. They are inexpensive and should be given the preference over the various nostrums that are not alone exploited as local antiseptics, but are also advertised as sure cure remedies for a number of intestinal disorders.

LIQUOR ANTISEPTICUS ALKALINUS, N. F., represents 3.2 parts each of potassium bicarbonate and sodium benzoate, 0.8 parts of sodium borate in a mixture of alcohol, glycerin and water, flavored with thymol, eucalyptol, oil of peppermint and oil of gaultheria and colored red with tincture of cudbear to make 100 parts.

tassium chlorate. This occurs in such a mixture as the following:

℞.	Potassii chloratis	ʒiss	6
	Acidi hydrochlor.	ʒi	4
	Aquæ q. s. ad	℥iii	100

M. Sig.: Use as a gargle.

After the use of any of these gargles the mouth should be well rinsed with water to prevent injury to the teeth.

The antisepsis of the nasal passages is usually accomplished by thorough cleansing with warm saline solution (0.9 per cent.), nine grams (135 grains) of sodium chlorid to a liter (quart) of water, or by a mild alkaline solution made by adding nine grams (135 grains) of sodium bicarbonate to the saline solution just mentioned; after which a mildly antiseptic solution, such as the official properly diluted, is used as a spray or douche, or, in lieu of this, one-tenth of 1 per cent. of phenol may be added to the saline douche, but the latter is not recommended as a routine practice.[5]

It may be permissible here to enumerate some of the substances that have been used as mild antiseptic applications to the mucous membranes.

ACIDUM BORICUM.—U. S. P.—Boric Acid, generally referred to as boracic acid, is quite free

5. The pharmacopeia of the German Hospital, Philadelphia, contains a formula for an alkaline antiseptic tablet that has found favor with some. It contains 0.25 gm. (about 4 grains) each of sodium bicarbonate, sodium borate, sodium chlorid and sodium phenolsulphonate with 0.005 gm. (about 0.1 minim) of oil of cinnamon. One of these tablets (the same mixture can also be directed in powder) is to be dissolved in six tablespoonfuls of recently boiled water and used as a wash for the nose.

from toxicity. It is soluble in about 16 parts of water and is but slowly absorbed.

GLYCERITUM BOROGLYCERINI.—U. S. P.—Glycerite of Boroglycerin, contains 30 per cent. of boric acid and has the same uses as that acid.

SODII BORAS.—U. S. P.—Sodium Borate, or borax, has an alkaline reaction and is sometimes preferred to boric acid on this account. It is soluble in sixteen parts of water.

SODII CHLORIDUM.—U. S. P.—Sodium Chlorid, common table salt, has been in use as an antiseptic from time immemorial; its uses are well known, and the only reason we have for presenting it here is to call attention to the fact that the Pharmacopeia recognizes it as a valuable article of the materia medica and provides certain standards and tests for purity.

SODII PHENOLSULPHONAS.—U. S. P.—Sodium Phenolsulphonate, the sodium sulphocarbolate of former editions of the Pharmacopeia, is another mild antiseptic that has limited but well-defined uses.

Practically all the salts of the alkalies have antiseptic properties, but it is obviously not necessary to recount all of them at this time.

Complete disinfection of the nose, mouth, throat, vagina and urethra is not practicable, and is not even necessary; the main thing to be sought is the cleansing of those regions from pus and organic matter on which bacteria thrive. Mucous membranes decompose the solution of hydrogen dioxid with such copious evolution of oxygen that it can not be used in the nose, and because of this rapid action by the mucous membrane itself a large

amount frequently repeated is necessary to completely disinfect such cavities.[6]

The antisepsis of the eye is confined largely to the use of camphor water, boric acid and sodium borate. In virulent affections more active antiseptics are sometimes indicated; in these cases weak solutions of mercuric chlorid, copper sulphate, zinc chlorid, silver nitrate or formaldehyd are used. These substances, however, are all extremely irritating and great caution is required. Their use by the general practitioner is not advised.[7]

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6. For use in the vagina, where a simple detergent and antiseptic action is sought, the official Liquor Cresolis Compositus in 0.5 to 1 per cent. solution will be found to be all that is required. When an astringent effect is desired the following formula for an antiseptic astringent powder will be found to answer the purpose very well:

℞.	Sodii boratis	℥i	60
	Alumin. exsicc	ʒx	40
	Thymol,		
	Phenol,		
	Eucalyptol,		
	Olei gaultheriæ, āā	gr. viii	5

M. Sig.: A heaping teaspoonful to be dissolved in one liter (1 quart) of hot water, to be used as a douche.

Pulvis Antisepticus, N. F., contains 12.5 parts of zinc sulphate, 86.6 parts of boric acid, 0.5 part of salicylic acid and 0.1 part, each, of phenol, eucalyptol, menthol and thymol. It may be used in the same way and for the same purposes as the prescription given above.

Tyree's Antiseptic Powder formerly had a considerable vogue among physicians; since the exposure of its true character by THE JOURNAL of the American Medical Association (Oct. 20, 1906, p. 1316), it is to be hoped that physicians will depend on it less than they did.

Campho-phenique Powder affords another example of extraordinary discrepancy between the formula claimed by the manufacturer and the composition shown by analysis. See THE JOURNAL A. M. A., April 20, 1907, p. 1365.

7. The method of using boric acid in the eye varies greatly, but usually a 2 per cent. solution of boric acid in equal parts of distilled water and camphor water will be found to be sufficient. When it is desired to use sodium borate in connection with boric acid the following will be found satisfactory:

℞.	Acidi borici	gr. xv	1
	Sodii boratis	gr. xxx	2
	Aquæ dest.,		
	Aquæ camphoræ, āā	℥iss	50

Burns or scalds resulting in destruction of the skin should be treated antiseptically. Treves directs that the burn be washed with a solution of hydrogen dioxid and then with a solution of boric acid; the vesicles are then opened with an aseptic needle and the surface dusted with iodoform and dressed with aseptic cotton.

POTASSII PERMANGANAS.—U. S. P.—Potassium Permanganate, already referred to under the head of general disinfectants, is often considered to be devoid of antiseptic properties because of the readiness with which it oxidizes all organic matter. It is true that potassium permanganate is readily decomposed by the organic matter with which it first comes in contact, and that it would be unusual indeed to find bacteria the only form of organic matter present in any one case. When we remember, however, that a very large number of bacteria represent but an infinitesimally small amount of organic matter, we will appreciate why potassium permanganate is capable of destroying vast numbers of micro-organisms in those cases in which its action can be confined to them.

This substance finds its greatest usefulness as a local application in rendering foul ulcers odorless. For this purpose a fairly strong solution, 2 per cent., is freely used as a wash. Much weaker solutions are sometimes used with great benefit as urethral irrigations in gonorrhea and as vaginal douches. A hot 1 per cent. solution of potassium permanganate will be found extremely useful as a deodorizer for instruments after use in the vagina while awaiting sterilization.

Potassium permanganate destroys some alkaloids much more quickly than others, e. g., morphin more readily than strychnin. It can not enter the circulation; hence, when swallowed, it can act only on the substances found in the stomach. Obviously it is not suited for hypodermic injections.

CHAPTER III.

INTERNAL ANTISEPTICS.

The great strides made in the use of antiseptics, after Lister had employed them in surgery with such brilliant results, led to the hope that they might be made available for limiting the development of bacteria in various parts of the human body. From time to time clinicians have reported favorable results from the use of internal antiseptics in such diseases as typhoid fever, but at the present time it is generally acknowledged that complete disinfection of the intestinal tract is impossible and that the treatment of constitutional diseases by means of antiseptics is possible only in a few isolated cases; for example, in malarial fever by quinin, in articular rheumatism by salicylic acid and its compounds, and in syphilis by means of mercurials. Quinin has been shown to have a peculiarly selective and destructive action on the protozoön which causes malarial fever, and perhaps mercury and salicylic acid may possess similar selective action against the agents producing syphilis and certain forms of rheumatism.

It is not probable that any agent will be found which will protect the blood and tissues against many species of bacteria, but we may discover substances, each with a specific action analogous to that of quinin in malaria. The discussion of internal antiseptics will be limited, therefore, to the substances just mentioned—quinin, mercury and

salicylic acid—and substances used as antiseptics in the alimentary canal.

It is impossible to form a correct idea of the probable effect of an internal antiseptic without having at least some idea of the organisms on which it must act.

Nuttall and Thierfelder took guinea-pigs from their mother by Cesarean section under aseptic conditions, and fed one of them on sterilized food for thirteen days, during which it continued to thrive, but Schotelius found that chickens died of starvation when fed only on sterilized food. G. N. Stewart accepts Nuttall and Thierfelder's results as demonstrating that animals, including man, exist, despite the bacteria which infest the alimentary canal from a few hours after birth until death.

Strassburger concludes, from a review of the extensive literature pertaining to intestinal bacteria, that Nuttall and Thierfelder have shown that no single process of alimentation is absolutely dependent on bacteria, but that the chief function of certain of them, notably the colon bacillus, which is always abundantly present, is actually to destroy other bacteria and thus to protect the host against those disease germs which may gain entrance to the alimentary canal. The destruction of all the bacteria in the alimentary canal at any one time, therefore, might prove fatal, in that any disease germs which chanced to gain access to the intestine could so multiply as quickly to destroy the life of the host.

The proof that bacteria do play some part in the process of digestion is found in the fact that man

can digest the cellulose of delicate vegetables to a limited extent, though he secretes no enzyme capable of splitting cellulose, which, therefore, must be split by bacteria present which have been shown to possess that power. Then, too, certain crystalline bodies other than leucin and tyrosin have recently been found among the ultimate products of digestion, and as none of the known digestive enzymes are capable of forming these bodies they likewise must result from bacterial action.

While we must admit that bacteria are concerned in digestion, we have no positive information at the present time as to how important a part they actually take. It has been shown that the colon bacillus, which is universally present in milk, inhibits, to a certain extent, the action of putrefactive bacteria, and it is well known that untreated milk of good quality is more digestible than is the same milk after sterilization.[1]

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1. Tests made on the several constituents of milk show that they have no power to inhibit putrefaction, though such a power is unquestionably possessed by fresh milk. That this is due, at least in part, to certain bacteria normally present in the milk is shown by the fact that sterilized milk putrefies much more rapidly than untreated milk on the addition of the bacillus of putrefaction (*B. putrificus*); but if with the *Bacillus putrificus* the colon bacillus be added to sterilized milk, the milk acts as does normal milk, thus proving that the colon bacillus is actually capable of inhibiting the development of certain bacteria. It is, of course, possible that fresh milk also possesses antibacterial properties which are destroyed by the sterilization. These conditions help to explain why sterilized milk is not so wholesome as new milk of good quality. It must be remembered, however, that milk is an excellent culture medium in which a great many bacteria are normally present, and that if it be allowed to stand in a warm place for some hours the micro-organisms multiply to such an extent that the milk is wholly unfit for use, and we do not wish to be misunderstood as implying that the colon bacillus is an unmixed blessing. Whilst during health the micro-organism probably does not emigrate from the uninjured intestine it may do so in states of lowered general resistance, or in the

We are thus forced, by this and other like evidence, to conclude that it is by no means desirable to render the intestines sterile and that, instead of attempting intestinal antisepsis in the broader sense, we should seek rather to modify the flora in that region than to destroy it.

Various methods have been proposed, from time to time, for determining the relative degree of putrefaction taking place in the intestines, but at the present time it is not positively known what constitutes the best method at our disposal for doing this. The procedure most frequently employed, one which is considered to afford a fair estimate in a large proportion of cases, consists in estimating the ethereal sulphates in the urine. Strassburger claims that weighing the bacteria after separation from the feces and drying affords the surest means of estimating the number of bacteria present. Others count the number of colonies which can be cultivated from a milligram of feces, but this has been shown to be unreliable. In view of the fact that laboratory methods are far from satisfactory in determining the number of the several varieties of bacteria present in the feces, the general practitioner will probably be obliged, for some time to come, to depend largely, if not entirely, on the clinical data presented by each individual case.

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presence of defects of the intestinal epithelium, and may give rise to blood infection, or more rarely to inflammations in various organs. The possibility that the bacillus of typhoid fever and kindred forms are only modified colon bacilli is of theoretical importance. Some authorities (Escherich and some others) deny that the colon bacillus is capable of rapidly becoming virulent. Different strains of the colon bacillus have different degrees of virulence, and it still remains possible that many cases of infantile colitis are caused by certain strains (*e. g.*, the colicolitis of Escherich).

Without knowing the precise rôle played by the multitudinous bacteria of many species, we do know in various ways when undue activity of the putrefactive bacteria occurs and certain symptoms give notice that excessive fermentation is taking place in the small intestine. A moderate increase in the number of colon bacilli tends to lessen the development of the putrefactive germs; on the other hand, an intestinal catarrh, caused by excessive acidity resulting from the undue fermentation of carbohydrates by the colon bacillus, may be alleviated by lessening the carbohydrates of the food and consequently the medium on which the colon bacillus thrives.

Normal peristalsis prevents undue development of bacteria by hurrying the food through the small intestine, but diarrhea and irritant purgatives favor the development of bacteria by the increased amount of liquid which is present, because of the increased secretion and diminished absorption. Thus more bacteria have been found after administration of calomel than were present before the drug had been given, though calomel is generally considered to be an excellent antiseptic.

While normal peristalsis limits the development of bacteria, the latter, in turn, liberate acids in the decomposition of carbohydrates which probably supply the stimulus which sets up peristalsis. The normal digestion and absorption of food also tend to lessen intestinal putrefaction by lessening the amount of material which can serve as a culture medium.

It is important that the intestinal wall should be kept intact. When the intestinal mucosa is in-

jured it fails to absorb the food products and the bacteria multiply rapidly. It has been found that many antiseptics injure the intestinal wall more than they do the bacteria, and, despite the fact that the antiseptic may be found in quantity in the feces when the bulk is small, it has actually permitted an increased growth of micro-organisms in the small intestine when other conditions favored the bacteria and not the antiseptic action. Strassburger found just double the number of bacteria after the use of naphthalene, which has been considerably lauded as an intestinal antiseptic.

As suggested before, the simplest means of diminishing the number of putrefactive bacteria is by lessening the amount of the proteid of the food. Though it has been contradicted by the indirect evidence of urinary constituents, it has been shown that the bacteria of the intestines are very much reduced in number by the withdrawal of all food.

It was formerly supposed that the gastric juice of the stomach interposed a fairly effective barrier to the entrance of living disease germs into the intestine, but this juice has but little effect at the beginning of digestion, when the activity is slight, and toward the end, when the hydrochloric acid is nearly all combined with proteid. Some micro-organisms, e. g., the tubercle bacillus, pass uninjured through the stomach more readily than others, e. g., the vibrio of cholera.

The effect of bile on bacteria is not positively known, but it is generally supposed that it does not possess any germicidal power, as some bacteria can be cultivated on bile, though not after the precipitation and removal of the mucus. The intestinal

secretion does not possess any germicidal power. All these factors are important, since all of them—bile, gastric juice and intestinal secretion—have at various times been supposed to possess antiseptic properties, and it is necessary to know what results are to be expected from increasing the quantity of any or all of them.

Strictly speaking, the antisepsis of the alimentary canal should begin with that of the mouth, but this is more conveniently considered under local antisepsis. In view of the fact that the gastric juice does not interpose an absolute barrier to the ingress of pathogenic bacteria to the intestine, the proper care of the mouth and the limitation of its flora assumes an added importance, and there is no question of the fact that proper attention to the cleanliness of the oral cavity will greatly lessen the danger from intestinal infection.

The general tone of these varied statements may appear pessimistic, so far as faith in the efficiency of intestinal antisepsis is concerned, but so far from that being the case they are intended to further demonstrate that our main reliance must, after all, be placed in guarding against the entry of disease-producing organisms into the alimentary canal and their destruction before they have passed beyond the reach of local treatment. After they have once gained admittance to the intestine the best means of limiting their development must be sought in regulating the diet and careful attention to the general condition.

If we are unable to destroy all or even any appreciable number of the bacteria of the intestine, it is consoling to know that some of them are our

allies instead of our foes. It is admitted by nearly all authorities that it is impossible to influence the bacillus of typhoid fever by antiseptics. It has been shown that a milk diet sometimes hinders the development of putrefactive bacteria, and many consider that the main benefit derived from a milk diet in typhoid fever is due to its effect on bacterial development. Fortunately, the *Bacillus typhosus* does not form spores and the bacillus itself is easily killed outside of the body; heating in water even to 75 C. (167 F.) for ten minutes greatly lessens its vitality.

It is practically impossible in the space at our disposal even to summarize the results of the hundreds of investigations dealing with the question of intestinal antisepsis. Those experiments which appear more nearly free from error point to the fact that we can not secure direct antiseptic action by chemical antiseptics in the intestine without injuring the intestinal wall, or at least materially reducing those conditions which naturally limit bacterial development, more than we injure the bacteria. The net result, therefore, is usually an actual increase of some species and a diminution of others. Clinical experience seems to prove conclusively that the mild mercurous chlorid, or calomel, is beneficial in those cases of indigestion which are characterized by that train of symptoms which includes a feeling of dulness, lassitude, headache, nausea and anorexia, the condition being popularly termed "biliousness." It is possible that the antiseptic action of the calomel, by limiting the development of other species of bacteria, gives the colon bacillus a chance to multiply, the increased amount of fluid

in the intestine having been found particularly to favor its development. These, in turn, may then modify digestion or serve to restrict the development of putrefactive bacteria, and, as we have seen, they favorably influence peristalsis, which in turn is one of the natural means of elimination of bacteria. The increased peristalsis caused by the calomel lessens the opportunity for absorption of the bacterial toxins which give rise to the train of symptoms mentioned; this lessened absorption may be due in part to the action of calomel on the wall of the intestine. This merely suggests the many-sidedness of an operation that appears at first glance to be a very simple one.

The action of the solution of hydrogen dioxid in the mouth and throat has been discussed under local antiseptics. Owing to the rapidity with which it is decomposed by mucous membranes, it can exert but little germicidal action in the stomach and absolutely none in the intestine or general circulation; indeed, it is so rapidly decomposed by the blood that it speedily causes death by embolism when introduced into the circulation. The same holds true of potassium permanganate, and it is probable that all antiseptics that depend for their action on the liberation of oxygen would be decomposed in the same way when brought in contact with the mucous membranes of the mouth and throat or the organic material necessarily present in the stomach.

ACIDUM HYDROCHLORICUM.—U. S. P.—Hydrochloric Acid, or muriatic acid, contains 31.9 per cent. of absolute hydrochloric acid. It is seldom used in medicine in this country, the preference being usually given to

ACIDUM HYDROCHLORICUM DILUTUM.—U. S. P. —Diluted Hydrochloric Acid, containing 10 per cent. of absolute hydrochloric acid. This acid undoubtedly exerts some germicidal action in the stomach when present in sufficient amount, and its action may directly influence the intestinal flora. It has been stated that the hydrochloric acid of the stomach becomes bound to albumin during digestion and then exerts no antiseptic influence, but we have also seen that normal digestion is one of the surest means of controlling the bacteria of the intestine, and how a deficiency of that acid may cause fermentative dyspepsia, with an enormous increase of bacteria, which may become virulent. It may be mentioned in this connection that, according to some recent experiments on man, the usual dose of dilute hydrochloric acid, 1 c.c. (15 minims) is entirely too small to supply the deficiency existing in many cases, and as much as 200 c.c. (6 fluid ounces) of 0.4 per cent. acid, corresponding to 10 c.c. of the official dilute acid, has been given with decided benefit when the usual dose or less had given no appreciable result. It must always be given diluted with a large amount of water. It should be remembered that mineral acids are to be taken through a tube to avoid injury to the teeth, and that the mouth should then be rinsed with water, or, better still, with a mild alkaline solution, such as limewater or a very dilute solution of sodium bicarbonate.

NAPHTHALENUM. — U. S. P. — Naphthalene, naphtalin and

BETANAPHTHOL. — U. S. P. — Betanaphthol and naphthol have been highly recommended as in-

testinal antiseptics. As we have seen, they do not usually lessen the number of bacteria, though they may exert a favorable, modifying action. These substances have been used in the treatment of diarrhea with excessive putrefaction. They are insoluble in water and are preferably directed to be dispensed in powder form, or dry, in capsules.

The average dose of naphthalene is given as 0.12 gm. (2 grains), and the average dose of betanaphthol as 0.25 gm. (4 grains). It has been suggested that naphthalene must be converted into betanaphthol before it can exert its antiseptic action, but even this point has not been satisfactorily determined.

There are a number of nostrums on the market consisting of betanaphthol combined with astringents, but in view of the complex nature of the problem with which we have here to deal it is preferable by far to employ the official substances, combining them as seems indicated in each case. To do this it is merely necessary to calculate the relative amount of each powder to be given at a dose and to dispense them either separately or in a single powder or a mixture.

Betanaphthol and bismuth subnitrate or subcarbonate may be combined somewhat as follows:

℞.	Bismuthi subnitratis	ʒi	4
	Betanaphthol	gr. xv	1

To be made into ten powders, one being given every two hours for diarrhea with foul-smelling feces.

℞.	Bismuthi subnitratis	ʒiiss	10
	Betanaphthol	ʒss	2
	Syrupi acaciæ	℥iss	50
	Aquæ camphoræ to make	℥iii	100

One teaspoonful to be given, after shaking, every two hours.

The number and variety of substances that have been suggested from time to time as intestinal antiseptics justifies a more extended review, but we can do little more than enumerate some of the official substances that have been used in the treatment of the several gastrointestinal disorders.[2]

Though it is impossible to secure asepsis of the intestinal tract by chemic means, lavage of the colon removes feces and vast numbers of bacteria which swarm in that region. Lavage is now pursued as a routine measure in diarrhea and dysentery. Proper attention must be paid to the technic of the operation, particularly with infants and small children, as serious harm may result from inattention to details, more especially in the matter of the temperature of the liquid and the pressure at which it is injected.

Normal saline or solution of boric acid is commonly used for the purpose; to this, opium may be added with caution in suitable cases, for instance, where there is much tenesmus.

The use of antiseptics in the treatment of typhoid and typhus fevers was first suggested in Germany more than thirty years ago, and the arguments that were offered at that time appeared so plausible that internal antiseptics at once sprang into vogue. Among the more popular were the following:

IODUM.—U. S. P.—Iodin is very seldom used as such at the present time.

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2. The following has been used to a considerable extent in the treatment of gastric fermentative dyspepsia, particularly when accompanied by nervous disturbances:

℞. Sodii bromidi ..... gr. v |3
Resorcinol ..... gr. ii |1
Aquæ anisi q. s. ad ..... ℥ii 10|

This dose to be taken after meals in half a glass of water.

Average dose: 0.005 gm. (5 mg., 1/10 grain).

LIQUOR IODI COMPOSITUS.—U.S.P.—Compound Solution of Iodin, better known as Lugol's solution, contains about 5 per cent. of iodin and 10 per cent. of potassium iodid in distilled water. This was at one time a favorite method of administering iodin.

Average dose: 0.2 c.c. (3 minims).

TINCTURA IODI.—U. S. P.—Tincture of Iodin is virutually a new preparation and combines the strength of the former official tincture with the water-soluble properties of the unofficial compound tinctures, or soluble iodin solutions. It contains 7 per cent. of iodin and 5 per cent. of potassium iodid in alcohol. This combination appears to conduce to stability and also permits of dilution with water, without precipitation.

Average dose: 0.1 c.c. (1½ minims).

Iodin and the water-soluble preparations of iodin were formerly much lauded as intestinal antiseptics, and even at the present time, though, as was shown in the introductory portion of this article, the practice is now obsolete, they are frequently exploited by manufacturers of nostrums as being little short of the ideal. The form in which iodin was formerly largely used was in connection with carbolic acid or phenol, thus:

℞. Tinct. iodi .....ʒiiss 10|
Phenol .....m. lxxv 5|
M. Sig.: ½ to 1½ minim three times a day in water.

Phenol[3] itself is now seldom employed, or even

3. The Phenol-sodique of Hance Brothers & White must not be confounded with that of the National Formulary, which possesses approximately one hundred times the phenol content of the nostrum. The false statements concerning their preparation made by that firm have been exposed in THE JOURNAL of Nov. 9, 1907, p. 1617. It is practically worthless for disinfectant purposes.

recommended, as an intestinal antiseptic, but the official phenol sulphonates, better known as sulphocarbolates, still have a number of ardent advocates.

SODII PHENOLSULPHONAS.—U. S. P.—Sodium Phenolsulphonate, the sodium sulphocarbolate of the previous Pharmacopeia.

Average dose 0.25 gm. (4 grains).

ZINCI PHENOLSULPHONAS.—U. S. P.—Zinc Phenolsulphonate is rather more active than the sodium salt, combining the astringent properties of the zinc with the antiseptic properties of the phenolsulphonic acid.

Average dose 0.12 gm. (2 grains).

Both the official salts are readily soluble in water and may be given in solution. Calcium phenolsulphonate is being lauded by some as an intestinal antiseptic, but there is no reason to believe that it offers any advantages over the sodium salt, and it is probably quite as harmless.

The following official derivatives, or substances coming directly under the same classification as phenol, are all comparatively insoluble in water and, for internal use, should be dispensed in capsules or in the form of emulsions or mixtures that are directed to be well shaken:

THYMOL.—U. S. P.

Average dose: 0.12 gm. (2 grains).

CREOSOTUM.—U. S. P.

Average dose 0.2 c.c. (3 minims).

GUAIACOL.—U. S. P.

Average dose: 0.5 c.c. (8 minims).

GUAIACOLIS CARBONAS.—U. S. P.

Average dose: 1 gm. (15 grains).

ACIDUM SALICYLICUM.—U. S. P.

Average dose: 0.50 gm. (7½ grains).

PHENYLIS SALICYLAS.—U. S. P.—Phenyl Salicylate, better known by its former official title, salol, is even now considered as being among the few really desirable or available internal antiseptics. It occurs as a white crystalline powder, having a faint but characteristic odor and a slight, rather peculiar taste; it is only slightly soluble in water, and, therefore, does not dissolve to any appreciable extent in the juices of the stomach. It is decomposed, however, by the alkaline liquids of the intestine into its constituents, phenol and salicylic acid, and thus becomes available as an antiseptic. It is said to be particularly useful in preventing the infection of the kidneys by the *Bacillus typhosus.*

Average dose: 0.50 gm. (7½ grains).

HEXAMETHYLENAMINA.—U. S. P.—Hexamethylentetramin will be discussed at greater length under diuretics (Chapter XVI). This substance has also been recommended as an available intestinal antiseptic, but, as noted under diuretics, the ultimate products of its decomposition are largely, if not entirely, eliminated by the kidneys, and it no doubt finds its greatest field of usefulness in preventing possible infection of the urinary organs.

Average dose: 0.25 gm. (4 grains).

It is manifestly impossible to discuss or even to mention all the agents that have been, or are, employed as intestinal antiseptics. Many of the remedies that are recommended as intestinal antiseptics are also useful as anthelmintics. Notable among these is thymol, which has been referred to frequently of late as being an efficient anthelmintic.

Though many efforts have been made to treat tuberculosis by means of internal antiseptics, the favorable influence which has so far been observed is to be attributed to the beneficial effects produced on the tissues, and not to any direct bactericidal action produced by the antiseptics themselves. Of the remedies that have been suggested for this purpose, creosote and guaiacol continue to be used, probably with some benefit.

The whole problem, however, appears to concern curative effect and treatment rather than antisepsis.

Few articles in our materia medica possess any action so specific as that shown by cinchona or its chief alkaloid, quinin, in the treatment of certain forms of malarial fever. Cinchona bark itself owes its introduction into Europe to the fact that it was found to be efficient in the treatment of fevers of a malarial type. For many years after its introduction into Spain the Jesuits had the bark sent to them by their brethren in Peru and carefully kept the source of its origin a secret, and the substance, therefore, became widely known as Jesuits' bark. Being virtually introduced as a nostrum, or secret remedy, it need not surprise us when we find that it has frequently taken a most important part as one of the component parts of a variety of nostrums, even down to our own times.

Quinin, the most valuable of the alkaloids of cinchona, was discovered by Pelletier and Caventou in 1820, and is to-day one of the few substances in medicine that has met with a constantly increasing popularity. Quinin is official under no less than six different titles, in addition to the several

scale salts and preparations that are not of direct interest in connection with its peculiar use in malarial fever, but which will be mentioned under the subject of bitters.

QUININA.—U. S. P.—Quinin.

QUININÆ BISULPHAS.—U. S. P.—Quinin bisulphate.

QUININÆ HYDROBROMIDUM.—U. S. P.—Quinin hydrobromid.

QUININÆ HYDROCHLORIDUM.—U. S. P.— Quinin hydrochlorid.

QUININÆ SALICYLAS.—U. S. P.—Quinin salicylate.

QUININÆ SULPHAS.—U. S. P.—Quinin sulphate.

Average dose of any of these preparations: 0.25 gm. (4 grains).

The physical properties of the several salts of quinin are so well known that they do not require a description at this time. The reasons for the popularity and use of some of these salts are not always apparent. In America the sulphate is used almost exclusively, while on the continent of Europe the hydrochlorid appears to be given the preference in nearly all cases. That each of the several official preparations of quinin has some particular point of merit is suggested by the following table, showing the relative percentage of anhydrous alkaloid quinin in each and also the relative solubility in water and in alcohol:

	Per cent. of anhydrous quinin.	Solubility in water.	Solubility in alcohol.
Quinin	85.5	1750.	0.6
Quinin bisulphate..	59.5	8.5	18.
Quinin hydrobromid.	76.6	40.	0.7
Quinin hydrochlorid.	81.5	18.	0.6
Quinin salicylate...	69.9	77.	11.
Quinin sulphate....	74.3	720.	86.

It will be noted that the very commonly used sulphate, next to the alkaloid itself, is the least soluble in water. This, while a decided advantage so far as masking the taste of the salt is concerned, is a marked disadvantage in attempting to make a solution of the salt. Where quinin sulphate is to be given in solution it must be given in an acid mixture or in solutions that are so dilute that the quantity to be taken would be nauseating.[4]

The more satisfactory method of administering quinin in the comparatively large quantities that are usually given is in cachets, gelatin capsules or pills.

The use of quinin as a destroyer of the protozoön which causes malarial fever is among the best established facts of therapeutics. It is mentioned here largely to avoid the criticism of incompleteness rather than to offer any suggestions of novelty to the general practitioner.

If fairly large doses of quinin be given four hours before the time at which the chill of malarial

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4. It is truly surprising that the sulphate of quinin continues to be used almost to the exclusion of the alkaloids and the other salts. When a tasteless mixture is desired the alkaloid is preferable because it is less soluble than any of the official salts; if it is necessary to administer the drug in solution ten grains of the hydrochlorid may be given in a teaspoonful of a mixture containing 50 per cent. of alcohol, while three grains of the hydrochlorid, or seven of the bisulphate may be given in a teaspoonful of a watery mixture. The following is a type of the usual acid mixture:

℞.	Quin. sulphatis	grs. lxxv	5
	Acid hydrochlorici dil.	m. lxxv	5
	Elix. aromat. q. s.	℥iii	100

When the salt, or better, the alkaloid, is to be given in a mixture, and the taste is to be masked, acids should never be added. Instead of the acid, a sweet substance, like glycyrrhizin, should be used to mask the bitter taste of the quinin. A satisfactory mixture is obtained as follows:

℞.	Quininæ vel quininæ sulphatis	grs. lxxv	5
	Fluid ext. glycyrrhizæ	ʒiv	15
	Syrupi et elix. aromat. āā q. s.	℥iii	100

fever is expected to occur, and the dose repeated in two hours, the maximum effect of the quinin on the organism is obtained and the chill is usually prevented. The quinin existing in the blood at the time that sporulation occurs destroys the newly liberated organisms and the blood is rendered aseptic so far as that particular organism is concerned. This process has to be repeated at intervals, sometimes for three or four weeks.

Salicylic acid is closely related, chemically and pharmacologically, to phenol. Salicylates of the alkalis are decomposed in the stomach and salicylic acid is liberated.

Salicylic acid is very slightly volatile; hence it does not penetrate so readily as phenol, and that property, non-volatility, explains its more lasting antiseptic action. It is much more potent than phenol in preventing the action of enzymes. It is irritant to mucous surfaces, often inducing nausea, but it is not nearly so caustic as phenol. Strong solutions applied to the skin cause the destruction of tissue, as in the case of warts and corns.

The salicylates are practically valueless as chologogues, though they may have some slight effect on the production of bile.

Salicylic acid and the salicylates cause increased metabolism and increased production of heat, but they also cause increased blood pressure and dilatation of the cutaneous vessels. The result of these two actions taken together is a greatly increased cutaneous circulation, with increased loss of heat and consequent fall in the temperature. This effect on the peripheral vessels may also explain the

rash sometimes observed after the use of the salicylates.

Salicylic acid circulates in the blood as sodium salicylate. This in sufficient concentration is an antiseptic, but the salt passes too rapidly from the intestine to permit of its acting beneficially there, and it is excreted from the blood so rapidly that it is never in sufficient concentration to possess any antiseptic action. The salicylates pass into nearly all the secretions of the body and are particularly abundant in the urine as salicyluric acid.

Gaglio explains the action of the salicylates in rheumatism by the rapid excretion into the joints by the synovial membrane by which the salt is secreted from the blood.

Salol, or phenyl salicylate, is much less soluble in water than is sodium salicylate. It is decomposed in the stomach very slowly, but much more rapidly in the intestine, with the liberation of phenol and salicylic acid. Owing to the slight solubility of salol in the stomach, it may be used to coat capsules of sodium salicylate which will then pass into the intestine without causing gastric disturbance. The liberated phenol exerts its action, and it may give rise to toxic symptoms if too large a dose of salol has been used.

Salicin is converted in part into salicylic acid when taken internally, but much of it escapes destruction and is excreted in the urine unchanged.

ACIDUM SALICYLICUM.—U. S. P.

Average dose 0.5 gm. (7½ grains).

SODII SALICYLAS.—U. S. P.

Average dose: 1 gm. (15 grains).

AMMONII SALICYLAS.—U. S. P.

Average dose: 0.25 gm. (4 grains).

LITHII SALICYLAS.—U. S. P.

Average dose: 1 gm. (15 grains).

STRONTII SALICYLAS.—U. S. P.

Average dose: 1 gm. (15 grains).

PHENYLIS SALICYLAS.—U. S. P.—Salol (U. S. P., 1890).

Average dose: 0.5 gm. (7½ grains).

METHYLIS SALICYLAS.—U. S. P.

Average dose: 1 c.c. (15 minims).

OLEUM BETULÆ.—U. S. P.

Average dose: 1 c.c. (15 minims).

OLEUM GAULTHERIÆ.—U. S. P.

Average dose: 1 c.c. (15 minims).

SALICINUM.—U. S. P.

Average dose: 1 gm. (15 grains).

The salicylates of ammonium, sodium lithium and strontium may be dispensed in solution, but the other salicylates and salicylic acid itself are best dispensed in capsules.

The salicylates were employed at one time as antipyretics, and they have also been used in place of quinin in malaria, but they have no curative value in that disease and are not so employed at present, having been superseded by less dangerous antipyretics.

In acute articular rheumatism the salicylates enjoy a reputation akin to that of quinin in malaria. As previously stated, they are excreted into the urine, and, as they exert their irritant action on the kidneys, they must be used only with great caution when renal inflammation exists, as they are capable of giving rise to the gravest symptoms. Whether the salicylates should be used when car-

diac symptoms arise is an unsettled question. They should certainly be used only with caution in such an event. Any of the salicylates may be used, but the sodium salt is much the most popular. Large doses are often necessary in the beginning of treatment, but these must be diminished as the symptoms of the disease abate.

Sodium salicylate may be prescribed as follows:

℞. Sodii salicylatis .....ʒiiss 10|
Ft. capsulæ No. xx.
Sig.: Two capsules every three hours.

It may be prescribed in liquid form somewhat as follows:

℞. Sodii salicylatis .....ʒiiss 10|
Syrupi aurantii .....fl℥iss 50|
Aquæ, q. s. ad.....fl℥iii 100|
Misce. Sig.: Two teaspoonfuls every three hours.

Such doses are too large for continued use, and are to be regulated according to the needs of the case.

The capsules may be coated with salol after the manner described on page 87 to prevent gastric disturbance. The oil of wintergreen or oil of sweet birch is sometimes borne for a time when the sodium salt causes nausea. These oils may be given in capsules mixed with a bland fixed oil.

The mercurials will be discussed under the subject of alteratives.

CHAPTER IV.

GENERAL TONICS.

Tonics are defined by Gould as "medicines or agents which promote nutrition and give tone to the system."

Since these conditions are met by any improvement in the general health, the use of the term is often an admission of our want of exact knowledge of the mode of action of the drugs or remedies so classed.

Strychnin increases the reflexes and may thus improve the muscular tone. Bitters may increase the impaired appetite and digestion, which will, of course, improve the general condition, hence these agents may be spoken of as tonics; and, if we were not acquainted with the organism which causes malarial fever, and with the effect of quinin on that organism, but merely knew this condition to be relieved by quinin, we would be justified in attributing the action to the tonic effect of quinin. Therefore, as our knowledge of the exact mode of action of the various remedies of this group increases, the importance of the term itself will correspondingly decline.

Among the tonics we may include hematinics, or agents which assist in the regeneration of blood, including iron, arsenic, codliver oil and hypophosphites; the alteratives, the mode of action of which is unknown, and stomachics.

HEMATINICS.

Ordinary food is the most important of the hematinics, if, indeed, we have any others which are of considerable importance, especially if we accept the definition which includes iron in any assimilable form as food.

IRON.

Most of the iron in the body, amounting to from 2½ to 3 grams (38 to 45 grains) occurs as a constituent of hemoglobin, an extremely complex substance in which the iron is much more firmly bound than in the ordinary iron albuminate. In addition to that found in the blood, some iron is held in reserve in the liver and spleen in the form of the ferratin of Schmiedeberg (not the commercial Ferratin) and the cells of the body also contain small amounts of iron.

The subject of the absorption and assimilation of iron has been the subject of many investigations, and the results have often proved contradictory, but it may be accepted now as definitely established that both the organic and the inorganic forms of iron are absorbed from the small intestine, that they are carried by the blood to the liver and the blood-building organs and are utilized in the formation of hemoglobin.[1]

This occurs even with doses of inorganic iron which are incapable of causing corrosion of the mucous membrane of the stomach prior to absorption.

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1. Prior to the discovery by Wöhler of the synthesis of such a comparatively simple substance as hippuric acid in the kidney it was supposed that no synthesis could occur in the animal body.

Dogs were rendered anemic by giving them food poor in iron and subjecting them to repeated hemorrhage. After the reserve iron of the liver was greatly diminished the animals were given the same kind of food poor in iron, but to the food of some was added iron in various forms, inorganic in some cases, organic in others. Those which received only the food poor in iron were unable to make good the loss of hemoglobin, but those receiving the same kind of food with the addition of any form of iron not only increased the hemoglobin of their blood, but added to the reserve store of the liver. Bunge's theory that inorganic iron is useful in chlorosis only because it combines with the hydrogen sulphid in the intestine and thus spares the iron of the food from being rendered non-absorbable, has been proved erroneous, as no hydrogen sulphid could be found in the duodenum, where iron is mainly absorbed, and the other heavy metals, such as bismuth, combine with hydrogen sulphid, but they have no such action as the inorganic salts of iron in anemia.

Even if Bunge's theory concerning the absorbability of organic forms of iron were correct his warning against the nostrums containing iron should not be forgotten. Bunge specifically states that meat and other foods are decidedly preferable to those preparations.

Abderhalden isolated from spinach a compound similar to hematogen, and Bunge's remarks apply with equal force to those preparations which contain iron of vegetable origin.

It has been shown that a part at least of the

organic iron[2] of the food is broken down into simpler forms during its passage through the intestinal wall. This and the fact that ferratin of the liver (the probable precursor of hemoglobin) is not so stable as the food iron, point strongly to the utilization of inorganic iron in the formation of hemoglobin.

While much diversity of opinion has been held concerning the precursor of hemoglobin, the question is of less therapeutic importance than it would seem at first thought, in view of the fact that it is a comparatively infrequent occurrence that a patient is unable to take a sufficient amount of iron in the food. We have devoted so much space to the subject mainly because the manufacturers of certain nostrums, used as hematinics, are prone to quote such results as those obtained in Bunge's laboratory only so far as they show that organic iron preparations are assimilable while the inorganic are not.

OFFICIAL PREPARATIONS OF IRON.

The list of official preparations of iron is a long one and comprises a number of substances that are not generally used as hematinics.

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2. Cushny: "Pharmacology and Therapeutics" says: "The words organic and inorganic in connection with these preparations have no reference to the combination to which iron is attached, but to the method of attachment. Thus the acetate and albuminate of iron are both classified among the inorganic iron compounds, because they are capable of dissociation, and the iron is precipitated by ammonium sulphid. Masked iron is a preferable term for organic iron, but has not been so widely used. A large number of the proteid compounds that have been introduced in the last few years promise to be relegated to merited oblivion in the near future. The albuminate of iron and the peptonate of iron are generally prepared by the action of the chlorid on egg albumin or on peptone, and differ very considerably in the percentage of iron. These preparations are not organic iron in the sense defined above, for the iron can be split off easily, and is precipitated by sulphids almost as readily as the ordinary salts."

The use of the salts of iron as astringents will be referred to in Chapter VIII.

Probably the most widely used of the several preparations of iron is

TINCTURA FERRI CHLORIDI.—U. S. P.—This preparation contains 35 per cent. by volume of solution of ferric chlorid. It should be prepared at least three months before being used. Tincture of ferric chlorid, or tincture of iron, as it was formerly called, has long been considered one of the most efficient of the inorganic iron preparations.

Average dose: 0.5 c.c. (8 minims).

FERRI SULPHAS AND FERRI SULPHAS GRANULATUS.—U. S. P.—These differ only in the size of the crystals; they consist of ferrous sulphate containing 7 molecules of water of crystallization. Ferrous sulphate is soluble in less than one part of water, but is insoluble in alcohol.

Average dose: 0.2 gm. (3 grains).

FERRI SULPHAS EXSICCATUS.—U. S. P.—Exsiccated Ferrous Sulphate is a grayish-white powder that is slowly but completely soluble in water. About 65 grams of the exsiccated preparation are equivalent to 100 grams of the granulated.

Average dose: 0.12 gm. (2 grains).

PILULÆ ALOES ET FERRI.—U. S. P.—Each pill contains 0.07 gm. (about 1 grain) each of exsiccated ferrous sulphate, purified aloes and aromatic powder.

Average dose: 2 pills.

PILULÆ FERRI CARBONATIS.—U. S. P.—This preparation is variously known as Blaud's pills, Griffith's pills or Vallet's pills. Each pill contains

about 0.06 gm. (1 grain) of ferrous carbonate, with potassium sulphate, althea, tragacanth and glycerin.

Average dose: 2 pills.

FERRI CARBONAS SACCHARATUS.—U. S. P.—The saccharated carbonate of iron should contain not less than 15 per cent. of ferrous carbonate.

Average dose: 0.25 gm. (4 grains).

MASSA FERRI CARBONATIS.—U. S. P.—Mass of ferrous carbonate, better known as Vallet's mass, contains nearly 5 per cent. of ferrous carbonate.

Average dose: 0.25 gm. (4 grains).

MISTURA FERRI COMPOSITA.—U. S. P.—Compound iron mixture, or Griffith's mixture, is much more popular in England than in this country. It contains freshly precipitated ferrous carbonate suspended in a mixture of potassium sulphate, myrrh, syrup, spirit of lavender and rose water.

Average dose: 16 c.c. (4 fluidrams).

Of the several official preparations containing ferrous carbonate the pill of ferrous carbonate, more generally known as Blaud's pill, is probably the most efficient and most satisfactory. This pill should be freshly prepared and should not contain free or unchanged ferrous sulphate or potassium carbonate. The practice that has been adopted by some manufacturers of massing these pills without allowing the chemical reaction to take place is a reprehensible one, as it is not at all probable that the necessary reaction will take place in the acid medium of the stomach.

Should a nascent ferrous carbonate be desired it can readily be provided by using the following solution:

Ferrous sulphate	**3.2 gm.**	**50 gr.**
Potassium carbonate	**1.6 gm.**	**25 gr.**
Distilled water	**2.0 c.c.**	**30 min.**
Glycerin to make	**100.0 c.c.**	**3 fl.oz.**

Dissolve the potassium carbonate in 45 c.c. of glycerin and add this to the solution of ferrous sulphate, made by dissolving the latter, by means of heat, in the water and subsequently diluting with 40 c.c. of glycerin. Finally, add sufficient glycerin to make the mixture measure 100 c.c.

Each teaspoonful (5 c.c.) of this mixture, when diluted with half a glass of water, will produce a quantity of freshly precipitated ferrous carbonate that is equivalent to one Blaud's pill.

All the preparations of ferrous carbonate have the decided advantage over the previously mentioned preparations of iron that they are not astringent and, therefore, are not likely to cause digestive disturbances.

Another preparation that is free from the objectionable feature of being astringent is:

FERRUM REDUCTUM.—U. S. P.—Reduced Iron occurs as a fine grayish-black lusterless powder without odor or taste. It is insoluble in water and in alcohol and, therefore, is generally directed to be dispensed in powders, capsules or pills.

Average dose: 0.05 gm. (1 grain).

SCALE SALTS OF IRON.

FERRI CITRAS.—U. S. P.—Ferric Citrate occurs in thin garnet-red scales that are slowly but completely soluble in water.

Average dose: 0.25 gm. (4 grains).

FERRI ET AMMONII CITRAS.—U. S. P.—Iron and Ammonium Citrate is much more freely solu-

ble in water than the simple citrate, an advantage that it is not likely to lose on keeping.

Average dose: 0.25 gm. (4 grains).

FERRI ET AMMONII TARTRAS.—U. S. P.—This occurs in thin transparent scales varying in color from garnet red to reddish brown. It is freely soluble in water, but insoluble in alcohol.

Average dose: 0.25 gm. (4 grains).

FERRI ET POTASSII TARTRAS.—U. S. P.—This is very similar in physical properties to iron and ammonium tartrate.

Average dose: 0.25 gm. (4 grains).

FERRI ET QUININÆ CITRAS.—U. S. P.—Iron and Quinin Citrate contains about 11.5 per cent. of quinin, and ferric citrate corresponding in amount to 13.5 per cent. of metallic iron. It is slowly but completely soluble in water.

Average dose: 0.25 gm. (4 grains).

FERRI ET QUININÆ CITRAS SOLUBILIS.—U. S. P.—This preparation has practically the same composition as iron and quinin citrate, but with ammonium citrate present to insure its solubility.

Average dose: 0.25 gm. (4 grains).

FERRI ET STRYCHNINÆ CITRAS.—U. S. P.—Iron and Strychnin Citrate contains about 1 per cent. of strychnin. It is readily and completely soluble in water.

Average dose: 0.12 gm. (2 grains).

These several scale preparations of iron are comparatively free from astringent properties, are generally freely soluble in water, do not attack the teeth, and are not obnoxious to the taste. They are preferably directed to be dispensed in aqueous

solution, with or without the addition of elixir or some other flavoring admixture.

LIQUID PREPARATIONS OF IRON.

VINUM FERRI.—U. S. P.—This contains 4 per cent. of iron and ammonium citrate with syrup and white wine, flavored with tincture of sweet orange peel.

Average dose: 8 c.c. (2 fluidrams).

VINUM FERRI AMARUM.—U. S. P.—This preparation contains 5 per cent. of soluble iron and quinin citrate with syrup and white wine, flavored with tincture of sweet orange peel.

Average dose: 8 c.c. (2 fluidrams).

GLYCERITUM FERRI QUININÆ ET STRYCHNINÆ PHOSPHATUM.—U. S. P.—The Glycerite of the Phosphates of Iron, Quinin and Strychnin contains 8 per cent. of the soluble ferric phosphate, 10 per cent. of quinin and 0.08 per cent. of strychnin with phosphoric acid, glycerin and water.

Average dose: 1 c.c. (15 minims).

SYRUPUS FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM.—U. S. P.—This syrup contains 25 per cent. of the glycerite of the phosphates of iron, quinin and strychnin in syrup.

Average dose: 4 c.c. (1 fluidram).

ELIXIR FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM.—U. S. P.—This popular ferruginous bitter tonic contains soluble ferric phosphate, quinin and strychnin. The average dose given below contains nearly 0.07 gm. (1/16 gr.) of soluble ferric phosphate, 0.035 gm. (7/12 gr.) of quinin, and 0.001 gm. (1/60 gr.) of strychnin.

Average dose: 4 c.c. (1 fluidram).

LIQUOR FERRI ET AMMONII ACETATIS.—U. S. P.—This Solution of Iron and Ammonium Acetate, more popularly known as Basham's mixture, contains a double salt of iron and ammonium acetate and is directed to be made by mixing 4 parts of tincture of ferric chlorid, 6 parts of diluted acetic acid, 50 parts of solution of ammonium acetate, 12 parts of aromatic elixir, 12 parts of glycerin and a sufficient quantity of water to make 100 parts. This preparation, being quite dilute, is not very stable and should be freshly prepared when wanted.

Average dose: 16 c.c. (4 fluidrams).

There are two additional preparations of iron that, while they are not prescribed as hematinics, might well be mentioned in this connection.

ANTIDOTES FOR ARSENIC.

FERRI HYDROXIDUM.—U. S. P.—This is the hydrated oxid of iron of the previous Pharmacopeia which is directed to be made by precipitating 100 parts of solution of ferric sulphate with 133 parts of ammonia water that has been diluted with 1,000 parts of cold distilled water. The resulting precipitate is directed to be washed until free from soluble sulphates. This preparation is not particularly adapted for extemporaneous preparation, and, as it does not keep well, the following has been added as an efficient, extemporaneous antidote for arsenic:

FERRI HYDROXIDUM CUM MAGNESII OXIDO.—U. S. P.—This is directed to be made by diluting 40 parts of solution of ferric sulphate with 125 parts of water, and kept in a large well-stoppered

bottle. The magnesia mixture is directed to be made by rubbing 10 parts of magnesium oxid with sufficient water to make a smooth and thin mixture, then diluting it to about 700 parts. When wanted for use the magnesium oxid mixture is to be well shaken and then gradually added to the solution of ferric sulphate, and the resulting mixture again well shaken.

Average dose: Arsenical antidote, 120 c.c. (4 fluidounces).

INDICATIONS FOR IRON.

Hematinics are demanded when the amount of blood or of any of its essential constituents have been greatly reduced.

After severe hemorrhage involving the loss of less than half the blood, regeneration takes place rapidly, if the general condition of the patient is otherwise good and the food ample.

Iron has long been used in chlorosis, and experience has shown that it is more useful in those forms of anemia in which the loss of hemoglobin is greater than that of red blood cells; in other words, when the red blood cells present, whether in normal or diminished number, are individually poor in hemoglobin.

As to the form of iron to be given, of first importance is the selection of food. Reference to the table given below will enable the physician to compute approximately the amount of food iron which the patient is receiving, and by computing the daily normal loss at 10 milligrams he can see about how much of this is left for the regeneration of hemo-

globin. The figures given are for material as usually served at table[3] and are only approximate.

If the food contains an insufficiency of iron, hematin, or one of the inorganic forms of iron will prove beneficial. In our choice of medicinal iron we must be guided by the individual case in selecting the one which causes the least disturbance of the digestion. In the absence of fever it will seldom occur that the patient can not take a selected diet containing an ample supply of iron. If the appetite and digestion are deficient, stomachics are indicated.

Inorganic iron very often gives better results in the first few weeks of the administration than it does later, which may possibly be explained by its interference with the digestion—a matter to be

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3. The following table is based on computations made by Bunge of the iron content in dried substances. The figures given here serve as an indication of the approximate content, in milligrams, in the amount of each article as ordinarily served at meals:

Teacupful of boiled oatmeal	0.2- 0.5
Teacupful of boiled rice	0.2- 0.5
500 gm. of grapes (about one pound)	0.4- 1.0
Two apples	0.1- 0.4
Two oranges	0.1- 0.5
Yolk of two eggs	2.0- 5.0
Glass of cow's milk	0.4- 1.0
Four small slices of white bread, about 100 gm	0.5- 1.0
Four slices of whole wheat bread	1.0- 3.0
Plate of pea soup, thick	0.4- 2.0
Slice of roast beef, about 50 gm	2.0- 6.0
Teacupful of mashed potato	0.3- 1.5
Teacupful of boiled cabbage	0.5- 3.0
Two heaping tablespoonfuls of spinach	2.0-10.0
Two heaping tablespoonfuls of boiled carrots	0.3- 1.5
Two heaping tablespoonfuls of string beans	0.4- 2.0
Two heaping tablespoonfuls of green peas	0.3- 1.5
Six to eight leaves of lettuce	0.1- 1.0
Four to six stalks of asparagus	0.5- 3.0
Ten or twelve almonds, blanched	1.0- 2.0
Ten or twelve almonds, whole	2.0- 5.0
Ten or twelve hazel nuts	1.0- 4.0
Four to six figs	0.5- 2.0
Slice of "blut-wurst," about 100 gm	10.0-25.0

Sugar and white of egg are free from iron.

guarded against carefully. Large doses, if they do not disturb the digestion, are often required.

While warm blood may be tolerated by some individuals, the aversion to it is frequently unconquerable and hematin seems to be equally serviceable in any case.[4]

The etiology of some of the anemias is so obscure that treatment must be mainly empirical, but we may feel reasonably certain that we shall do more harm than good if we depend on the nostrums so glowingly advertised instead of directing our efforts toward improving the appetite and digestion. The selection of a proper diet, together with proper doses of inorganic iron in most cases, or of organic and inorganic iron in comparatively few cases in which they are needed, will usually be found to be all that is required.

When iron tends to cause constipation, laxatives must be employed, preferably one of the preparations of cascara sagrada, or the pills of aloes and iron, one of which may be given three times daily.

As examples of the innumerable combinations in which iron may be prescribed we give the following:

℞. Ferri sulphatis exsic.....ʒi 4|
Extracti nucis vom. |
Extracti rhamni pursh., āā....gr. xv 1|
M. Ft. pil. No. lx.
Sig.: One pill half an hour after meals.

Reduced iron or ferric citrate may be substituted for the dried ferrous sulphate, and a slightly larger amount of aloes (20 grains—1.3 gm.) can be used in place of the extract of cascara sagrada.

4. A practical method for the economic preparation of a hematin product was described by Torald Sollmann, in the Am. Jour. of Phar., June, 1902, p. 275.

Clinical experience seems to show that a formula of this kind is not so useful in those conditions in which there is a deficiency of hydrochloric acid in the gastric secretions; in such cases small doses, from half to one teaspoonful, of the solution of iron and ammonium acetate may be given, after meals. This preparation rarely gives rise to constipation or other symptoms of indigestion. It is not very stable and should be dispensed in small amounts.

The pills of ferrous carbonate, Blaud's pills, may be given either alone, or the mass of ferrous carbonate, which is practically identical, may be used in combination with such a laxative as the extract of cascara sagrada, in the dose mentioned above. If desirable a bitter substance such as the extract of nux vomica may also be included as follows:

℞.	Massæ ferri carbonatis .....ʒii	8 |
	Extracti nucis vom.	|
	Extracti rhamni pursh., āā....gr. xv	1 |

M. Ft. pil. No. lx.

Sig.: One pill half an hour after eating.

Other bitter extracts, or other bitter substances, such as quinin or strychnin, and other laxatives may be substituted for those given above. A representative formula for a pill of this general composition would be as follows:

℞.	Ferri reducti	|
	Quininæ sulphatis	|
	Aloes purificat, āā.....gr. xlv	3 |
	Strychninæ sulph .....gr. i	| 06
	Ext. gentian q. s.	|

M. Ft. pil. No. lx.

Sig.: One pill three times a day after eating.

While it is true that the salts of the alkaloids might be substituted by the alkaloids themselves,

the amount of acid present is so small that it is really of very little moment.

In this same connection it may be pointed out that the dried ferrous sulphate or the ferric citrate may be substituted for the reduced iron, or, by omitting the extract of gentian, the mixture may be directed to be dispensed as a powder in capsules.

The tincture of ferric chlorid is best given well diluted with water, a glass tube being used to prevent the corrosive action of the acid on the teeth, and the mouth should then be well rinsed with water, or a dilute solution of an alkali such as lime water.

The scale salts of iron, being generally combinations with organic acids, are much less corrosive than the chlorid, or either of the sulphates, and may frequently be used with advantage in their stead. A representative formula for a simple solution of this kind would be as follows:

℞.	Ferri et ammonii citratis	ʒi	4
	Aquæ dest	fld. ʒxii	50
	Elixir q. s. ad	fld. ℥iii	100

M. Sig.: One teaspoonful three times a day before eating.

Any one of the soluble scale salts of iron can be substituted for the iron and ammonium citrate, and one of the aromatic waters can be used in place of the distilled water, or of the water and the elixir.

The official bitter wine of iron, given a few minutes before meals, is an excellent ferruginous stimulant of the appetite and digestion which women will usually find acceptable.

MANGANESE.

Manganese is not absorbed in appreciable amounts from the alimentary canal after medicinal doses. Its use as a hematinic is based on its supposed property of neutralizing the hydrogen sulphid in the intestine, and thus sparing the iron of the food, but the fallacy of this theory has been mentioned. Manganese would, therefore, not be mentioned here if it were not for its widespread use, thanks mainly to the methods used in exploiting the nostrums containing it.

The report of the Commission for the Study and Treatment of Anemia in Porto Rico was published by the government of that island in December, 1904. This report, which was the subject of editorial comment in THE JOURNAL of the American Medical Association, confirms the use of inorganic iron in anemia.

The misuse of this report by the M. J. Breitenbach Company furnishes an example of the distortion of facts by nostrum makers to suit personal ends. THE JOURNAL of Sept. 23 and Oct. 7, 1905, exposed this misrepresentation of the report of the commission, and later it gave a careful analysis of a report of the use of Gude's Pepto-mangan in 32 cases of anemia in the Infants' Hospital on Randall's Island. The analysis is brief and convincing and will repay perusal by any one who uses that nostrum.

The so-called peptonized manganese preparations, generally solutions of peptone to which some salt of manganese has been added, may be obtained from reputable dealers in pharmaceuticals, or may be made by any retail pharmacist who has the

necessary educational qualifications to conduct even the very simplest chemical experiments.

Peptonates were introduced, upwards of twenty years ago, by E. Dietrich, who published detailed directions for preparing them. His formulas have frequently been republished, and his processes are sufficiently simple to be followed by even a tyro. A number of manufacturers in this country and abroad have adopted them, and not a few of the proprietary preparations now on the market, consisting of variable mixtures of iron, manganese and peptone, are but poor substitutes for the original preparation proposed by Dietrich.

The commercial dry peptonates are not elegant preparations, and physicians who are desirous of avoiding the use of proprietary articles will do well to have their neighboring pharmacist prepare for them a solution of the peptonates according to Dietrich's original formula, or the modification, proposed by Dunning, in the Proceedings of the American Pharmaceutical Association for 1905.

OFFICIAL PREPARATIONS OF MANGANESE.

The official preparations of manganese are limited in number, and, as suggested above, are even more limited in their practical application as tonics or hematinics; they are:

MANGANI DIOXIDUM PRÆCIPITATUM.—U. S. P. —Precipitated Manganese Dioxid is a new preparation that has been added to replace the crude product formerly official. Manganese dioxid is directed to be made from manganese sulphate and should contain not less than 80 per cent. of manganese dioxid.

Average dose: 0.25 gm. (4 grains).

MANGANI SULPHAS.—U. S. P.—This occurs as colorless or pale pink crystals that are soluble in less than one part of water, but insoluble in alcohol.

Average dose: 0.25 gm. (4 grains).

POTASSII PERMANGANAS.—U. S. P.—This substance has been mentioned in the chapters on disinfectants and antiseptics. In connection with tonics or hematinics it is of interest only as the source of some of the now popular organic preparations of manganese.

ARSENIC.

It is not positively known whether arsenic is an essential constituent of the human body or not.

Segale, using penicillium brevicaule, with which infinitesimal quantities of arsenic may be detected, found it widely distributed in animal tissues, and Bertrand found it in eggs, particularly in the yolk.

Wieser concluded that arsenic is not a constant constituent in animal and human tissues, but that it is accidentally present.

When one considers the distribution of arsenic in plants, in sea water and in many springs, it is apparent that abundant opportunity occurs for its entrance into the body, and, owing to its slow excretion, the organism may rarely be without traces of it.

If minute traces of arsenic are essential to the well-being of the body we may be sure that the ordinary food insures an abundant supply.

Gies found that those members of a litter of rabbits which received arsenic grew faster than the others, while female rabbits under its influence bore larger young. This increased rapidity of

growth has been observed by some, but not all, subsequent investigators. In this connection the observation of arsenic in the yolk of egg is at least suggestive.

The toxicology of arsenic is of peculiar interest because of its frequent use with fatal effect and because the appearance of the earliest symptom is used as a guide in its therapeutic use.

The most striking effect of acute arsenical poisoning is seen in the symptoms closely resembling those of Asiatic cholera, which are explainable by the characteristic action on the capillaries, particularly those of the abdominal region.

The capillaries appear to suffer a peculiar paralysis and dilation, resulting in an enormous increase in permeability. The escaping plasma of the blood makes its way into the intestine, and, coagulating, gives rise to the "rice-water" stools. The withdrawal of the blood from the rest of the body into this region and its loss, as mentioned, causes the usual symptoms of collapse.

The direct effects on the heart are too slight in such cases to be considered important, and the corrosive action of arsenic is too slowly developed to be concerned in the immediate effects just described, which rapidly follow the absorption of a poisonous dose. When the poisoning is more slowly developed, however, as after frequently repeated smaller doses, catarrh of the gastrointestinal tract is seen and fatty degeneration of various organs takes place, the picture somewhat resembling that seen after phosphorus poisoning.

Even therapeutic doses frequently repeated give

rise to effusion of liquid, commonly noticeable in the swollen eyelids.

Arsenic is said to be capable of increasing the number of erythrocytes in anemia through its action on the bone marrow, but Engel found no increase in the mature red blood cells in anemia; other observers failed to see any change in the red blood cells or in the hemoglobin.

It has been claimed that arsenic actually diminishes the number of red blood cells in chlorosis without altering the total amount of hemoglobin.

It has been suggested that the influence of arsenic on metabolism is due to alternate reduction and oxidation, arsenous and arsenic acids being repeatedly formed, but this seems hardly probable.

Arsenic is, in part, excreted in the urine, feces and other excretions, but a part is stored in various organs of the body.

Heffter could find but little arsenic in the bones after long-continued administration; this is contrary to the theory that arsenate of calcium may replace the phosphate in bones.

An arsenical powder containing as high as 0.3 per cent. of arsenic may be obtained by causing yeast to grow in increasing concentrations of arsenic.

The organic compounds, including cacodylic acid and its salts, are less poisonous than the inorganic compounds, because the arsenic is more firmly bound and, for the same reason, they are less effective therapeutically. They are poisonous. however. It has been erroneously stated that atoxyl (which is the sodium salt of para-aminophenyl arsenic acid) can be given in doses fifty times as great as those of the inorganic salts.

OFFICIAL PREPARATIONS OF ARSENIC.

ARSENI TRIOXIDUM.—U. S. P.—Arsenic Trioxid was formerly official as Acidum Arsenosum. It consists of not less than 99.8 per cent. of pure arsenic trioxid. It may occur in transparent masses, like glass, or in opaque masses, resembling porcelain; more frequently, however, it is found as an odorless and tasteless white powder that is slowly but completely soluble in 100 parts of water, but very sparingly soluble in alcohol. The presence of either alkalies or halogen acids facilitates the solution of arsenic trioxid, and this fact is taken advantage of in the preparation of the several official solutions. White arsenic, as it is still called, was not known in Europe until some time after the eleventh century. It was scarcely well defined until 1733, when Brandt accurately determined its nature and leading chemical properties.

Average dose: 0.002 gm. (2 mg. or 1/30 grain).

ARSENI IODIDUM.—U. S. P.—Arsenous Iodid occurs as an orange red, inodorous crystalline powder. It is soluble with partial decomposition, in about 12 parts of water and in about 28 parts of alcohol.

Average dose: 0.005 gm. (5 mg. or 1/10 grain).

SODII ARSENAS.—U. S. P.—This occurs as colorless, transparent, odorless prisms that are soluble in less than two parts of water, but very sparingly soluble in alcohol.

Average dose: 0.005 gm. (5 mg. or 1/10 grain).

SODII ARSENAS EXSICCATUS.—U. S. P.—This should contain not less than 98 per cent. of pure anhydrous di-sodium-ortho arsenate. It occurs as an amorphous white powder, permanent in dry

air; it is soluble in about three parts of water and is practically double the strength of the hydrous or cystalline preparation mentioned above.

Average dose: 0.003 gm. (3 mg. or 1/20 grain).

SOLUTIONS OF ARSENIC.

While several of the preparations of arsenic appear to have been used from time immemorial as topical applications, the internal use of arsenic, in Europe, appears to date from the introduction of the solution of potassium arsenite, popularly known as Fowler's solution, about 1786. During the following decades a number of modifications of this solution of arsenic were suggested by medical practitioners and apothecaries, all of which had, or were supposed to have, some distinctive properties. Of these almost innumerable solutions that have been proposed during the past century, the following are now official:

LIQUOR POTASSII ARSENITIS.—U. S. P.—The Solution of Potassium Arsenite, universally known as Fowler's solution, as noted above, was the first of the several solutions to be used and is even now the most popular, being known in every civilized country in the world.

Solution of potassium arsenite contains the equivalent of 1 per cent. of arsenic trioxid, with a sufficient amount of the compound tincture of lavender to give the preparation a distinctive color and flavor.

Average dose: 0.2 c.c. (3 minims).

LIQUOR ACIDI ARSENOSI.—U. S. P.—This Solution of Arsenous Acid contains the equivalent of 1 per cent. of arsenic trioxid, with 5 per cent. of

diluted hydrochloric acid. This preparation was introduced about the end of the eighteenth century by Dr. De Valanquin, in London; it was the first of the several acid preparations of arsenic.

Average dose: 0.2 c.c. (3 minims).

LIQUOR ARSENI ET HYDRARGYRI IODIDI—U. S. P.—This preparation, more popularly known as Donovan's solution, contains 1 per cent. each of arsenous iodid and mercuric iodid.

Average dose: 0.1 c.c. (1½ minims).

LIQUOR SODII ARSENATIS.—U. S. P.—This Solution of Sodium Arsenate, also known as Pearson's solution, contains 1 per cent. of exsiccated sodium arsenate.

Average dose: 0.2 c.c. (3 minims).

Solutions of arsenic containing a bromid have also had their advocates, in times gone by, and several of these are still used to some extent. The present edition of the National Formulary contains two formulas for preparations of this type:

LIQUOR POTASSII ARSENATIS ET BROMIDI.—N. F. This preparation, at one time widely known as Clemen's Solution, represents the equivalent of 1 per cent. of arsenic trioxid in combination, probably as arsenate, and bromid of potassium.

Average dose: 0.2 c.c. (3 minims).

LIQUOR AURI ET ARSENI BROMIDI.—N. F.—Solution of bromid of gold and arsenic represents in each 0.6 c.c. (10 minims) 0.002 (2 mg. 1/32 grain) of tribromid of gold and the equivalent of 0.005 (5 mg. 1/13 grain) of tribromid of arsenic.

Average dose: 0.2 c.c. (3 minims).

The several solutions of arsenic are best administered with simple diluents, and not in complex

mixtures. Arsenic trioxid and other arsenic compounds may also be given to advantage in pill form.

THERAPEUTICS OF ARSENIC.

While the probability of favorably influencing nutrition under certain conditions, by means of the action of arsenic on the capillaries, can not be doubted, its therapeutic use for such purposes is empirical. The use of arsenic as a local caustic has a rational basis, but that will not be discussed here.

Arsenic has long been used in the treatment of a great variety of complaints in which anemia is a prominent symptom. Among these conditions is remittent fever, in which it is given in connection with quinin. It is preferable to give the two separately, arsenic being used in the form of the solution of potassium arsenite, which has a wide range of pharmaceutic incompatibility. This solution may be given in large doses—ten drops—gradually reduced, or in small doses rapidly increased until intestinal symptoms or swelling of the eyelids is seen, after which the drug is to be discontinued for a time, and then given in doses of from three to five drops three times a day. It is of importance that the dosage be watched so that no serious disturbance of digestion may occur. The frequently made suggestion to combine preparations of opium with the preparation of arsenic, so as to establish a tolerance for the latter, is one that is of doubtful utility in view of the fact that opium would be likely to mask the symptoms that occur as forerunners of more serious disturbances.

In chlorosis, arsenic seems to be useful in connection with iron. The combination most fre-

quently prescribed is a pill of ferrous carbonate with arsenic trioxid. For this purpose the latter may be combined with the official pill, or the mass of ferrous carbonate, as follows:

℞. Massæ ferri carbonatis.....ʒi 4|
Arseni trioxidi .....gr. i |05
M. et div. in pil No. xl.
Sig.: One pill three or four times a day.

Pernicious anemia may show some temporary improvement under arsenical treatment, but the effect is not permanent.

The use of arsenic in diseases caused by trypanosomes, particularly the "sleeping sickness," has attracted considerable attention of late.

It has been said that lymphosarcoma has shown improvement under its use, and the following conditions are enumerated among those in which it has been employed: Dyspepsia, diseases of the skin dependent on nutritional derangements, cachectic conditions resulting from diabetes, tuberculosis and a number of other more or less well-defined diseases.

The use of arsenic among veterinary surgeons for improving the appearance of horses by increasing the glossiness of the hair and adding to the fat under the skin is well known.

PHOSPHORUS.

Phosphorus, in both inorganic and organic combination, is widely distributed in the body. Lecithin, a compound of cholin with phosphoric and fatty acids, occurs in nearly all living animal and vegetable tissues, while the nucleins, which are also rich in phosphorus, are likewise widely distributed.

While some observers have found that when lecithin or nuclein was added to the food of animals the latter grew faster than the controls which were not given these compounds, these results are not universally accepted as proving their value, and we have the classic research of Miescher, which proves that the animal organism is abundantly able to form those compounds from others normally existing in the body.

Miescher found that the mass of eggs in the salmon increased from 0.4 per cent. to from 19 to 37 per cent. of the total body weight during some months when the salmon took no food, while the muscles showed a corresponding loss in weight. Much more nuclein and lecithin are found in the eggs than previously existed in the muscle, which, however, are rich in other phosphoric-acid compounds, probably potassium salts which are loosely bound to the proteid.

Miescher concludes, and the evidence seems incontrovertible, that the newly formed combinations characteristic of the egg (including lecithin and nuclein) are formed by chemic action from the albumin, fat and phosphates of the muscle.

It will be seen how the makers of nostrums can use such results as those quoted in regard to the action of lecithin in causing an increase in the body weight, while the much more important and generally accepted results of Miescher are ignored.

The presence in the brain and nerves of an abundance of compounds rich in phosphorus has led to the mistaken idea that their physiologic importance is an index of the therapeutic value of organic and inorganic preparations of phosphorus.

Lecithin and nuclein have been extravagantly lauded in the treatment of the greatest variety of diseases, but who would venture to attribute extraordinary curative properties to eggs used in doses of one-fourth of the yolk of one egg, yet the yolk of an egg does actually contain enough lecithin for four ordinary doses, or about 1.8 gm. (28 gr.) in a perfectly available form.

Nuclein and lecithin are very widely distributed, and our food always contains much more than the amounts advised for therapeutic administration.

Phosphorus and its preparations might be omitted without serious detriment to this chapter, but for the fact that they have been so widely used and, therefore, require at least a passing notice, particularly as the toxicology of phosphorus is of considerable interest.

The heart suffers greater direct injury in phosphorus poisoning than does any other organ, while the accumulation of fat which it causes in the liver is apparently an infiltration, resulting from a peculiar disturbance of metabolism rather than the result of any change in the organ itself.

Hemorrhages may occur from degeneration of the capillary walls, while a similar effect on the mucous membranes of the stomach and intestine causes pain, vomiting and diarrhea.

Minute doses of phosphorus, long continued, induce a peculiar change in the growth of the bones in the young, leading to the deposition of dense bone where cancellous is being formed, or the change of the latter, when already formed, into the compact form.

The phosphates are of the very greatest importance in the plant and animal bodies, but they occur so abundantly in the soil and in ordinary food that there is seldom any deficiency in the supply, and any want of them in the human body must be due to the inability to use that which is offered. Schmiedeberg calls attention to the formation of the egg shell as evidence of the great capacity of the animal organism to supply a special demand.

Sollmann states that there is absolutely no scientific foundation for the popular belief that the hypophosphites improve nutrition in anemia and beginning phthisis, while Cushny states that most reliable investigators deny that they have any other influence on nutrition and digestion than that of the better known and cheaper salts of lime, soda or iron, and Schmeideberg appears to think them entirely unworthy of notice.

Many clinicians, on the other hand, appear to have observed a distinct improvement in the appetite and digestion under the influence of the hypophosphites, but, even if such is the case, there seems to be absolutely no reason or excuse for our employing such a high-priced, unsightly and unscientific preparation as the muddy-looking Fellows' syrup, since any competent pharmacist can make a more presentable and more satisfactory preparation at a very much smaller cost.

The official preparations of phosphorus in its different forms afford evidence of the necessity for more careful scrutiny of the scientific claims of medicinal preparations before admitting them to the Pharmacopeia, if it is to command the support

of scientific and progressive physicians rather than pander to a numerous, though less, discerning clientage.

OFFICIAL PREPARATIONS OF PHOSPHORUS.

PHOSPHORUS.—U. S. P.—A translucent, nearly colorless solid, having at ordinary temperatures about the consistency of beeswax.

Phosphorus is nearly insoluble in water, but is soluble in 350 parts of alcohol and in 50 parts of a fatty oil.

Average dose: 0.0005 gm. (0.5 mg. 1/128 grain).

PILULÆ PHOSPHORI.—U. S. P.—Each pill contains 0.0006 gm. (0.6 mg. 1/100 grain).

Average dose: 1 pill.

ACIDUM PHOSPHORICUM.—U. S. P.—This contains 85 per cent. of absolute orthophosphoric acid. It is usually prescribed as:

ACIDUM PHOSPHORICUM DILUTUM.—U. S. P. —This contains 10 per cent. of absolute orthophosphoric acid.

Average dose: 2 c.c. (30 minims).

Phosphoric acid has many of the properties of other (inorganic) acids, and probably has no evident advantage over them as a tonic.

The official salts of phosphoric acid usually partake of the properties of the base rather than the acid, and need not be mentioned in this connection.

ACIDUM HYPOPHOSPHOROSUM.—U. S. P.—This contains 30 per cent. of absolute hypophosphorous acid and is chiefly used in preparing:

ACIDUM HYPOPHOSPHOROSUM DILUTUM.—U. S. P.—This contains 10 per cent. of absolute hypophosphorous acid.

Average dose: 0.5 c.c. (8 minims).

The official salts of hypophosphorous acid are:

CALCII HYPOPHOSPHIS.—U. S. P.

POTASSII HYPOPHOSPHIS.—U. S. P.

SODII HYPOPHOSPHIS.—U. S. P.

Average dose of any one of the above: 0.50 gm. (7½ grains).

Potassium hypophosphite is soluble in about 0.5 part of water and in 25 parts of alcohol, and calcium hypophosphite is soluble in about 7 parts of water, but is almost insoluble in alcohol.

In addition to the alkali hypophosphites, we also have official:

FERRI HYPOPHOSPHIS.—U. S. P.—and:

MANGANI HYPOPHOSPHIS.—U. S. P.

Average dose of either: 0.20 gm. (3 grains).

The ferric hypophosphite is soluble in 2,300 parts of water, but is much more readily soluble in solutions of hypophosphorous acid and the alkali citrates. Manganese hypophosphite is soluble in about 7 parts of water.

SYRUPUS HYPOPHOSPHITUM.—U. S. P.—Syrup of hypophosphites contains in 100 c.c. 4.5 gm. of calcium hypophosphite and 1.5 gm. each of sodium and of potassium hypophosphites.

Average dose: 8 c.c. (2 fluidrams).

SYRUPUS HYPOPHOSPHITUM COMPOSITUS.—U. S. P.—Compound Syrup of Hypophosphites contains, in each average dose (8 c.c. = 2 fluidrams) about 0.25 gm. (4 grains) of calcium hypophos-

phite, 0.12 gm. (2 grains) each of potassium hypophosphite and of sodium hypophosphite, 0.015 gm. (¼ grain) each of ferric hypophosphite and of manganese hypophosphite, 0.008 gm. (⅛ grain) of quinin, 0.0008 gm. (1/80 grain) of strychnin with sodium citrate, hypophosphorous acid and syrup.

Average dose: 8 c.c. (2 fluidrams).

SYRUPUS CALCII LACTOPHOSPHATIS.—U. S. P. —This syrup contains in 100 c.c. about 3 gm. of calcium lactophosphate with free lactic and phosphoric acids.

Average dose: 8 c.c. (2 fluidrams).

The several salts of glycerophosphoric acid which are being advertised so extensively at the present time, as the active constituents of a number of nostrums are, as yet, not official. The chemistry of the glycerophosphates is, however, well understood, and there is no reason why any reliable pharmacist can not supply preparations containing them. The third edition of the National Formulary includes the formula for an elixir that may be considered as being typical of this class of preparation.

Elixir Glycerophosphatum, N. F. The average dose, 4 c.c. (1 fluidram) contains 0.065 (1 grain) of sodium glycerophosphate and 0.032 (½ grain) of calcium glycerophosphate.

THERAPEUTICS OF PHOSPHORUS AND ITS SALTS.

There is at least a rational basis for the use of phosphorus in rickets, osteomalacia and fracture of bones in which union fails to occur, since a deposition of lime salts in bone has been shown to result from its use.

It must not be given in doses large enough to cause serious gastrointestinal disturbance.

When we say that phosphorus or the hypophosphites are used empirically in the following conditions it is not to be understood that we recommend them, but merely that they may possibly be worthy of a trial. Thus some clinicians have used phosphorus in a variety of nervous disorders, and the hypophosphites are very often used as general tonics. The treatment of tuberculosis by the hypophosphites has no place in modern therapeutics.

Phosphorus is so slightly soluble in water that it was formerly often used dissolved in oil, but the phosphorated oil is no longer official. The pills of phosphorus, each containing 0.6 milligrams (1/100 grain) afford a very convenient form for administration.

The compound syrup of the hypophosphites, with its eleven ingredients, including water, affords an example of the concessions made, by the revision committee of the Pharmacopeia, to popular prejudice, and it should be dropped at the next revision.

The claim has been made that the hypophosphites are effective only when the chemically pure salts are used; this claim, however, seems scarcely credible in view of the fact that our ordinary food contains much greater quantities of just such salts as are said to render the hypophosphites useless.

From one to two teaspoonfuls of the compound syrup of the hypophosphites may be given before meals, as a stimulant to the appetite and digestion. Acids and acid fruits are to be avoided.

The following may be taken as a type formula for an extemporaneous preparation of the hypophosphites:

℞.	Calcii hypophosphitis	
	Sodii hypophosphitis	
	Potassii hypophosphitis, āā.....ʒi	4
	Acidi hypophosphorosi .....ʒi	4
	Aquæ dest .....℥iv	120
	Elixir q. s. ad.....℥viii	250
	M. et filtra.	

Sig.: One or two teaspoonfuls three times a day before eating.

The elixir in this preparation may be replaced by glycerin, or an aromatic water, the combination of the hypophosphites may be varied, within reasonable limits, and the hypophosphorous acid substituted by citric acid or by an alkali citrate. When desirable sufficient bitter may be added to make the medicine more palatable or to act as a bitter tonic. For this purpose the tincture of nux vomica, or one of the bitter alkaloids, may be added.

COD-LIVER OIL.

The consideration of cod-liver oil rightly belongs under the subject of dietetics, as nearly all pharmacologists are agreed that it is merely a food, but it is so frequently lauded as a medicine that some mention of it is necessary in this place.

On the discovery of traces of certain alkaloids or ptomains it was suggested that they possessed extraordinary value, but, as these substances are usually present in infinitesimally small and varying quantities in good oil, and as there is no reason to suppose that they possess any beneficial effect whatsoever, it can not be said that the so-

called fat free or tasteless preparations can represent cod-liver oil in any sense of the word.

The crude dark-colored oil often contains a much larger proportion of free fatty acids than the white does, and it should, therefore, be more readily emulsified in the intestine and absorbed, but its disagreeable odor and taste render it peculiarly disgusting to patients with delicate stomachs. Small doses of cod-liver oil can usually be borne, especially if it be given in the form of an emulsion, but even this is not always tolerated.

OFFICIAL PREPARATIONS OF COD-LIVER OIL.

OLEUM MORRHUÆ.—U. S. P.—This preparation is official in some of the foreign pharmacopeias as Oleum Jecoris Aselli, a name that may be useful on occasion. Cod-liver oil is a fixed oil obtained from the fresh livers of *Gadus morrhuæ* and of other species of *Gadus*.

Average dose: 15 c.c. (4 fluidrams).

EMULSUM OLEI MORRHUÆ.—U. S. P.—The Emulsion of Cod-liver Oil contains 50 per cent. of the oil, with mucilage and syrup, and is flavored with oil of gaultheria.

Average dose: 8 c.c. (2 fluidrams).

EMULSUM OLEI MORRHUÆ CUM HYPOPHOSPHITIBUS.—U. S. P.—This contains 50 per cent. of cod-liver oil, 1 per cent. of calcium hypophosphite, and 0.5 per cent. each of potassium hypophosphite and of sodium hypophosphite. It is flavored with oil of gaultheria.

Average dose: 8 c.c. (2 fluidrams).

Cod-liver oil is often useful in anemias due to faulty nutrition and in the general debility which

so often precedes tuberculosis. For this reason, perhaps, it has acquired a particular reputation in the treatment of tuberculosis. It can have no specific action on the bacillus of tuberculosis, or on the course of the disease, except in so far as it is a readily assimilable food.

It is often found to be useful in rickets. The pure oil, the emulsion, or the emulsion with hypophosphites may be used, the dose to be regulated according to the capacity for assimilation of the individual case.

It may be added here that the petroleum oils alone, or in the form of emulsions, are wholly devoid of nutrient properties. They are mineral oils, and, therefore, non-saponifiable and can take no part in animal nutrition.

CHAPTER V.

ALTERATIVES.

Alterative is a term somewhat loosely applied to tonics, which, in some unknown way, favorably influence the processes of nutrition which have been disturbed by disease. They include hematinics, the various preparations of mercury, and many, if not all, the preparations containing iodin, either free or in combination.

A number of drugs of vegetable origin, such as sarsaparilla, were formerly classed as alteratives, but these are, for the most part, merely purgatives, or else devoid of therapeutic interest.

The use of the thyroid gland in thyroid disease and in obesity, and of the newly discovered serum of Beebe in exophthalmic goiter, have a scientific basis, but the employment of iodids in rheumatism and in syphilis, and of the mercurials in the latter disease is empirical, and in this connection the pharmacology of these agents is of minor importance since it throws little light on their therapeutic application.

While the attempts to investigate the action of these agents have not led to satisfactory results, we may refer to the conclusions of J. Levi, who sought to compare the effect of mercurials and of potassium iodid on the metabolism and on the blood of syphilitics. He used potassium iodid and various organic and inorganic preparations of

mercury in the second stage of the disease in 252 patients.

Levi found that mercurials increase organic combustion and hasten metabolism in this condition. With the gradual disappearance of the disease the processes of nutrition improve, but relapses are frequent. He found no evidence, however, of a specific influence on the micro-organism of syphilis, but according to the most recent view mercury is antagonistic to this micro-organism.

If the use of mercurials be too greatly prolonged the number of red blood corpuscles is diminished. Levi found that potassium iodid had a similar general influence on the nutrition of syphilitics. While it causes an increase in the body weight, improves the blood, and adds to the muscular strength, it retards combustion and lessens metabolism. He explains its uses in tertiary syphilis by supposing that it neutralizes the disease products without increasing organic combustion.

Nearly all observers are agreed that the action of mercurials is almost wholly independent of the preparation chosen, the only essential for its action being that it shall be absorbed. Mercury probably circulates as an albuminate, which is soluble in the blood because of the excess of proteids and chlorids which it encounters there.

Owing to the obscurity of many of the symptoms of syphilis, and also to the fact that a comparatively large number of people are not willing to have it known to their physician that they suffer with such a loathsome disease, the condition is peculiarly favorable for the practice of charla-

tans. While there is no disease that more urgently demands the skill and judgment of the specialist, there is none, perhaps, that is so frequently treated by incompetents and even by patients themselves.

While we have always with us the humiliating spectacle of numerous nostrums ostensibly advertised only to the medical profession, some of them of vegetable origin and wholly worthless in syphilis, others consisting of one form or another of mercury and possessing few or no advantages over the old and better known official mercurials, we are also daily confronted with advertisements which disgrace our boasted civilization in that they seek to persuade the deluded victims to palter with the use of nostrums in the vain effort to treat themselves.

MERCURY AND THE MERCURIALS.

HYDRARGYRUM.—U. S. P.—Mercury, or quicksilver, has been known from remote antiquity, and from the earliest times it has played an important part, not alone in the industries, arts and superstitions, but also in the medical practices of the people who were acquainted with it.

It is widely used for external application as well as for internal administration in the form of preparations produced by mechanical subdivision of the mercury. Several of the preparations of mercury have been mentioned under other headings, and we shall only mention a few of the salient features of these several substances.

HYDRARGYRUM CUM CRETA.—U. S. P.—Mercury with Chalk, also known as gray powder, rep-

resents 38 per cent. of metallic mercury, with clarified honey and prepared chalk.

Average dose: 0.25 gm. (4 grains).

MASSA HYDRARGYRI.—U. S. P.—Mass of Mercury, better known as blue mass, contains 33 per cent. of metallic mercury, with glycyrrhiza, althæa, glycerin and honey of roses. An analogous preparation without glycerin is frequently found in the shops under the somewhat incongruous title, "Powdered Blue Mass."

Average dose: 0.25 gm. (4 grains).

The mass of mercury and the mercury with chalk are widely used as mild mercurials and are especially popular for use with children.

Being insoluble in water, they are not readily adapted for use in liquid form. Mixtures, of which the following formula is typical, are, however, used extensively for small children:

℞.	Massæ hydrargyri	
	Sodii bicarbonatis, āā.....gr. xxx	2
	Syrupi rhei aromat. q. s. ad.....f℥iii	100

Misce.

Sig.: Shake well. Give one-half or one teaspoonful from one to three times a day, according to age and condition of patient.

Probably the most widely used as well as the most popular of all the preparations of mercury as an antisyphilitic is:

HYDRARGYRI IODIDUM FLAVUM.—U. S. P.—Yellow Mercurous Iodid occurs as a bright yellow, amorphous powder, without odor or taste, and is practically insoluble in water and in alcohol.

Average dose: 0.01 gm. (10 mg. or 1/5 grain).

HYDRARGYRI IODIDUM RUBRUM.—U. S. P.—Red Mercuric Iodid occurs as a scarlet-red, amorphous

powder that is nearly insoluble in water, but soluble in 116 parts of alcohol; it is also soluble in solutions of the soluble iodids and in solution of mercuric chlorid.

Average dose: 0.003 gm. (3 mg. or 1/20 grain).

HYDRARGYRI CHLORIDUM CORROSIVUM.—U. S. P.—Corrosive Mercuric Chlorid, more popularly known as corrosive sublimate, has been used by the Chinese from a very early period. It was used by the early Arabian physicians, and a process for its production was described by Geber in the eighth century.

Mercuric chlorid occurs as colorless, rhombic crystals or crystalline masses, or, more frequently, as a white powder, and is odorless, but has an acrid and persistent metallic taste. It is soluble in about thirteen parts of water and in five parts of alcohol, more freely soluble in solutions of the alkaline chlorids.

Average dose: 0.003 gm. (3 mg. or 1/20 grain).

HYDRARGYRI CHLORIDUM MITE.—U. S. P.—Mild Mercurous Chlorid, better known as calomel, has been known to some of the eastern peoples from a very early period. It appears to have been introduced in Europe about the beginning of the seventeenth century. This substance occurs as a heavy white powder, without odor and practically without taste, and is insoluble in water and in alcohol.

Average dose as an alterative: 0.05 gm. (1 grain).

The Pharmacopeia includes several additional compounds of mercury, but as they are not used

for internal administration they need not be enumerated in this connection.

USES OF MERCURIALS.

Since the use of mercury as an alterative is largely limited to those conditions resulting from syphilis, either acquired or congenital, we shall at present confine ourselves to discussing its employment in this way.

The pathology of syphilis is very often so obscure that it should be treated by the specialist when possible, and the following is intended for the general practitioner who finds himself compelled to undertake the treatment of such cases.

There are many distinct symptoms that are manifested by patients with a syphilitic history which fail to respond to the treatment which is commonly successful with persons otherwise healthy, but which at once disappear when mercury is given.

Many authorities are opposed to any form of constitutional treatment for the first stage of syphilis because we have no specific capable of aborting the disease, and the treatment may mask or even prevent the appearance of those symptoms which render the diagnosis absolutely positive, without preventing the ultimate effects of the disease, thus condemning the patient to the hardships of a long and painful course of treatment without positive knowledge of its necessity. Others rely on their ability to diagnose syphilis by the chancre and the history of the case, and proceed at once to the use of mercury.

Inasmuch as it is supposed that mercury has comparatively little immediate influence on the

course of the disease at this time, we should be very sure of the correctness of our diagnosis before beginning a course of treatment which, to be effective, must be continued for many months, and is in itself not free from danger to the patient's health.

All mercurials are irritant when dissolved and there are serious objections to all the different available methods of administration. Chief among these objections is the disturbance of digestion, which is not wholly obviated even when the mercury is injected hypodermically or applied by inunction.

Diarrhea is often a troublesome result, for which opium is sometimes used, but the evils attending its use are obvious and its presence should always be suspected in nostrums containing well-known mercurials that are advertised as being guaranteed not to cause diarrhea or other gastric disturbances. Mercury is eliminated by all the channels of excretion and the kidneys not infrequently suffer serious injury. It follows that we must try to find the method best suited to the individual case, and attention is directed to the following means of administration with some of the objections to be guarded against or at least kept in mind:

It is generally agreed that since there is no essential difference between the action of the various organic and inorganic salts of mercury in syphilitic conditions, we should be guided in our choice of agent by the method of administration which experience teaches us to be best suited to the individual case. If the digestion suffers from the internal administration of mercurials, intramuscular injec-

tions may be tried; if these are too painful, inunction may be resorted to; but whatever method is followed we must be alert for the appearance of untoward effects and the diet must be the object of especial attention, one being selected which is nutritious while it is easily digested.

The mercurials are to be avoided or used only with great caution in cachexia due to other causes than syphilis, as their tendency to disturb digestion may increase the trouble.

They must be used only with the greatest caution in acute nephritis, but they seem to be less deleterious in the chronic form, though here, too, their action must be carefully observed.

Mercury is particularly potent for harm in pregnancy, especially in the latter months; abortion may occur or the child may suffer from mercurial poisoning.

For internal use either mercurous or mercuric iodid is usually preferred. The combination of mercuric chlorid with potassium iodid merely means the giving of mercuric and potassium iodids, as the reaction occurs as soon as the two substances are brought into contact. When the mercuric chlorid is used it is best given alone in the form of a pill or in dilute solution, as it is incompatible with a great many substances.

Mercuric chlorid may be given (really as mercuric iodid) as follows:

℞.	Hydrargyri chloridi cor.....gr. iii	20
	Potassii iodidi .....gr. x	60
	Aquæ dest., q. s. ad.....fl℥iii	100

M. Sig.: Ten drops in water after each meal. Increase each dose daily by one drop until symptoms of mercurialism are noted, then reduce to one-half.

This is not given as an example of the so-called mixed treatment, the dose of potassium iodid being entirely too small to be effective.

An example of a prescription for mixed treatment would be as follows:

℞.	Hydrargyri chloridi cor.....gr. i		05
	Potassii iodidi .....ʒiiss	10	
	Aquæ dest., q. s. ad.....flʒiii	100	

M. Sig.: One teaspoonful after each meal.

The object of giving the mercurials after meals is to insure the protection of the stomach, which the presence of food affords, against the irritant action of the metal.

The menstruum or diluent for the prescription for mixed treatment may be varied in a number of ways. The water may be substituted by any one of the medicated waters, by adjuvant elixir, aromatic elixir, compound tincture of gentian, compound syrup of sarsaparilla, or by a mixture of one or more of these vehicles; the most important point to be guarded against is the attempt to combine the potassium and mercuric iodid with alkaloids in solution, as the mixture of potassium and mercuric iodids is one of the most effective of precipitants for alkaloids.

The characteristic effects of mercury are to be carefully watched for and when the gums become slightly tender the dose is to be reduced somewhat in amount and given but twice a day—after the morning and evening meals. It would be well to wash down the dose with milk, the proteid of which will serve to protect the stomach against the irritant action of the mercury.

Mercurous iodid is not so corrosive as the mercuric, or red iodid, and it is often given in pill

form with some colloidal substance, such as extract of gentian.

The following is an example of this method of giving it:

℞. Hydrargyri iodidi flav. .....gr. vi |40
Extracti gentianæ .....gr. lx 4|
M. Fiant pilulæ No. xl.
Sig.: One pill after eating.

This dose may be gradually increased by giving two pills after the mid-day meal, and then two twice, and finally three times, a day until the symptoms of mercurialism mentioned above are seen. The dose is then reduced, as in the case of mercuric iodid, and given after the principal meals.

The mild mercurous chlorid, or calomel, may be used, but it is so insoluble that it is impossible to regulate the amount that is absorbed. Next to the administration of mercurials by the mouth, the intramuscular injection is to be preferred, but it causes great pain and may result in abscess formation unless caution is observed. The addition of cocain hydrochlorid has been recommended by some authorities, but we should bear in mind the danger of forming a habit which is, if anything, even more terrible than syphilis.

The injections should never be into or under the skin, but always deep, into the fasciæ, and should be made by the physician, as the patient can not be trusted to do it satisfactorily.

Insoluble mercuric salicylate is not infrequently used for intramuscular injections and, by many specialists, is considered to be the best preparation for this purpose.

It is claimed that the local irritation is much less marked and that abscess formation is much

less frequent. Mercuric salicylate is given suspended in oil or liquid petrolatum of such a strength that 0.6 c.c. (10 minims) represent 0.06 gm. (1 grain). The injections are usually given in the buttocks, care being taken that the same area is not selected for consecutive injections.

The first dose is usually 0.03 gm. (½ grain) given once or twice a week, and this is increased slowly to 0.10 gm. (1½ grains) or until the desired effect is obtained.

The advantages that are claimed for the injection of the insoluble salt are its slow absorption, the prevention of salivation, the accurate regulation of the dose and the more perfect control of the patient.

The inunction method is very commonly employed in the establishments at Hot Springs, Ark., where many syphilitics are treated.

The inunction may be done as follows: After inducing diaphoresis, 3 grams (about 45 grains) of mercurial ointment are rubbed into the skin, not merely on it, daily. As this must be applied to a rather large extent of surface it is customary to select six regions which are utilized on successive days, returning on the seventh day to the first region. These are the adductor surfaces of the thighs (the most convenient when the patient is to rub the ointment into his person), the armpits and the regions just below, extending anteriorly. and the subscapular regions of each side.

The ointments of the oxids of mercury and the oleate of mercury are more irritant than the mercurial ointment or the blue ointment, as the diluted mercurial ointment is now called.

Too much stress can not be placed on the necessity of giving close attention to the various bodily functions during the mercurial treatment, to maintain the appetite and digestion unimpaired, to regulate the bowels and to secure scrupulous cleanliness of the body. The mouth should be the object of especial attention; carious teeth should be filled and the mouth and teeth kept thoroughly cleaned. The systemic action of iodin and the iodids is very similar and they may be considered together.

The use of iodin and the iodids, like that of mercury, is well established on clinical evidence and we can only speculate as to the way in which it produces its effects in syphilis, chronic rheumatism and asthma, but the symptoms induced by their use require consideration.

Iodin, and more frequently the iodids, give rise to iodism; this occurs under very variable conditions. It may be induced by very small doses of any iodid, but disappear even when the dose is increased, or it may appear only when a certain amount is exceeded. The symptoms vary in intensity from a slight catarrh of the respiratory passages to grave, and even rarely fatal involvement of the larynx. The throat, tonsils and salivary glands are often affected, and a brassy taste in the mouth may be the first symptom observed by the patient. Headaches may occur, the eyes become inflamed and various skin eruptions appear.

The iodids are decomposed in the tissues to a certain extent, and it is probable that the symptoms of iodism may be explained by the irritant action of the liberated iodin, and it has been suggested

that this liberated iodin also destroys the gumma occurring in syphilis.

Iodin and the iodids may cause nausea from the local irritant action in the stomach. They cause an increase in the iodothyrin of the thyroid gland, and this may explain their beneficial action in simple enlargement of the thyroid (goiter) as well as the untoward symptoms which sometimes follow its use in that affection, since the iodothyrin formed may suddenly liberate an unusual amount of the glandular secretion.

The mode of action of the iodids on the elimination of lead and mercury from the tissues is unknown, nor can we explain their action in aneurism, for it is not true that they slow the circulation of the blood by their action on the heart or by dilating the vessels.

The iodids are extremely diffusible and very soon after being taken they appear in the urine and other excretions and secretions of the body.

It has been suggested that a deficiency of thyroid secretion may sometimes predispose to aneurism and that the action of the iodids is dependent on their effects on that gland, but syphilis is known to be an extremely common antecedent to aneurism and that probably is the commonest explanation of the action of the iodids in that condition.

OFFICIAL PREPARATIONS.

IODUM.—U. S. P.—Iodin occurs in bluish-black rhombic plates that have a metallic luster, a distinctive odor and a sharp and acrid taste. It is only slightly soluble (1/5000) in water, but is readily soluble in ten parts of alcohol. It is also

soluble in an aqueous solution of potassium, or of sodium, iodid.

Iodin was discovered about 1812 by Courtois, a French manufacturing chemist, but it was not used in medicine until after 1820.

Average dose: 0.005 gm. (5 mg. or 1/10 grain).

LIQUOR IODI COMPOSITUS.—U. S. P.—Compound Solution of Iodin contains 5 per cent. of iodin and 10 per cent. of potassium iodid in distilled water.

Average dose: 0.20 c.c. (3 minims).

TINCTURA IODI.—U. S. P.—Tincture of Iodin, as now official, represents an alcoholic solution of 7 per cent. of iodin and 5 per cent. of potassium iodid. The resulting tincture is freely miscible with water and with alcohol.

Average dose: 0.10 c.c. (1½ minims).

ACIDUM HYDRIODICUM DILUTUM.—U. S. P.—This is a new addition to the Pharmacopeia and is intended primarily for the preparation of the syrup of hydriodic acid. It should contain not less than 10 per cent. by weight of the absolute acid.

Average dose: 0.50 c.c. (8 minims).

SYRUPUS ACIDI HYDRIODICI.—U. S. P.—This is a clear, colorless, syrupy liquid that contains about 1 per cent. of absolute hydriodic acid.

Average dose: 4 c.c. (1 fluidram).

Syrup of hydriodic acid is designed to be freshly prepared and the official requirements insure a uniformly elegant and efficient preparation.

SYRUPUS FERRI IODIDI.—U. S. P.—This syrup, in harmony with the Brussels conference agree-

ment, now contains about 5 per cent. by weight, of ferrous iodid.

Average dose: 1 c.c. (15 minims).

The official salts of iodin are all freely soluble in water and are also soluble in alcohol and alcoholic liquids. They are, in the order of their popularity and use:

POTASSII IODIDUM.—U. S. P.

SODII IODIDUM.—U. S. P.

STRONTII IODIDUM.—U. S. P.

Average dose of any of the above: 0.50 gm. (7½ grains).

AMMONII IODIDUM.—U. S. P.

Average dose: 0.25 gm. (4 grains).

While mercury is employed in all stages of syphilis, but is most useful in the second stage, the iodids are employed in the second and third stages, but find their greatest field of usefulness in the third. The iodids enjoy a peculiar reputation in the treatment of those symptoms of tertiary syphilis, such as periostitis, which are manifested in connection with the bones.

Potassium iodid is sometimes used in enormous doses—50 to 65 grams (800 to 1,000 grains) daily —in gumma of the brain and in cerebral syphilis, in which prompt action is necessary, the effect at times being truly remarkable in the promptness with which the symptoms improve.

Bronchitis, in those who suffer with a rheumatic or gouty diathesis, often shows greater improvement under the influence of this drug than with any other treatment.

The iodids are rarely used alone in the second stage of syphilis, but in combination with mercury,

known as the mixed treatment, already referred to, they appear to be of value.

The saturated solution of potassium iodid is, perhaps, the form of administration most commonly used.

The preparation of this may be entrusted to the pharmacist or it may be ordered as follows:

℞. Potassii iodidi .....ʒi 30|
Aquæ dest. q. s. ad.....fʒi 30|
M. Ft. solut.
Sig.: Five drops after each meal, the dose to be increased by one drop each day.

The increase in the amount to be taken may be continued until the symptoms of iodism arise or until sixty drops or more are taken daily.

The patient is to be instructed as to the symptoms to be expected, such as pain in the region of the parotid gland, etc.

The appearance of mild symptoms of iodism is not always the signal for stopping the iodids, as they may disappear if the dose is diminished and at times even when increased if this previously has been small. The symptoms of iodism nearly always disappear promptly when the iodids are withdrawn.

The iodids are often useful in the greatest variety of conditions occurring in syphilitics, or those with a syphilitic history, and their use should also be borne in mind always when such patients are being treated.

It is of little consequence whether we choose potassium iodid or one of the other inorganic iodids or an organic preparation. Potassium iodid has long been the most popular of all of the avail-

able preparations and will probably continue to be the most useful or, at least, the most frequently used.

THYROID GLAND.

The removal of the thyroid glands gives rise to certain symptoms like those seen in myxedema; it is evident that these symptoms are due to a deficiency in some glandular secretion, and it was soon found that myxedema could be successfully treated by the administration of thyroid in various ways. The active substance resists digestion and it was not long before its isolation was accomplished. It proved to be a non-proteid compound containing variable amounts of iodin according to the process of preparation. This iodin compound, called iodothyrin, probably represents fully the therapeutic activity of the gland.

Small doses of the gland or of iodothyrin have no effect on many normal individuals, but they sometimes cause disagreeable symptoms; these are more common in persons suffering with myxedema, palpitation of the heart being among the most common of these symptoms.

Iodothyrin is said to cause a fall of blood pressure when it is injected into a vein, but it is denied that the blood pressure is affected at all when iodothyrin or the gland substance is taken in the stomach.

Thyroid feeding causes a loss of weight in myxedema, and as a rule when first used for obesity, though the beneficial effects are usually temporary in the latter affection. This loss of weight is attributable in part to a destruction of fat, and in part to destruction of proteid. The patient can

be kept in nitrogen equilibrium while losing weight by a diet consisting largely of meat or other proteid. Thyroid feeding also causes diuresis and a part of the loss in weight may be attributed to the water separated from the tissues.

GLANDULÆ THYROIDEÆ SICCÆ.—U. S. P.—Desiccated thyroid gland is officially described as "the cleaned, dried and powdered thyroid glands of the sheep, freed from fat." It occurs as a yellowish amorphous powder, having a peculiar odor; it contains the active ingredients of the thyroid tissue. It is partially soluble in water.

Average dose: 0.25 gm. (4 grains).

Thyroid gland or iodothyrin is indicated in obesity, after removal of the thyroid or when the latter, through disease, fails to function properly, as in myxedema and in hypoplastic follicular goiter, but they must be used cautiously in myxedema, particularly when the heart becomes rapid and weak.

While they have been said to act beneficially in some cases of exophthalmic goiter, they usually augment the symptoms, and must be used only with extreme caution if at all.

CHAPTER VI.

STOMACHICS.

In this group are included a number of agents, many of them used for centuries, with actions scarcely better understood now than they were in the remote past. They include those agents commonly called bitters and aromatics, terms which refer only to taste, or, to be more accurate in the case of aromatics, to taste and smell, but which are employed as therapeutic terms for want of better, thus suggesting how little we know of their mode of action. Despite this want of exact knowledge of their pharmacologic action, the accumulated clinical evidence of 2,000 years or more goes to show that they are useful in slight catarrhal conditions and in minor functional disturbances of the alimentary canal in which there are no serious anatomic changes.

It is possible that their beneficial influence is sometimes due in part to the psychic effect, as they are agreeable to many tastes, and their regular use may encourage the patient—two important factors in digestion.

Most of the experiments that have hitherto been conducted with these agents have been made on animals, and the results have been variable and often contradictory, hence we must depend almost entirely on clinical evidence for guiding us in their uses.

Owing to the great variability of the functions involved and the natural discrepancy in the capability of various observers, most inaccurate conclusions have been reached, and, therefore, no attempt can be made to give precise information as to the exact relative merits of one member rather than another in a given condition.

That the taste of bitter substances excites the flow of saliva is a matter of common experience, and the bitter taste in the mouth of the dog has been found to cause a prompt, but not long-continued secretion of gastric juice. It is, therefore, advisable that bitter stomachics be taken, in liquid form, only a few minutes before eating. Bitter substances in pill form pass into the stomach with but little action on the latter organ and have little direct influence on the appetite.

After therapeutic doses of the simple bitters have reached the stomach they can hardly exert any perceptible effect directly on the activity of the gastric juice, and this extremely slight effect, if adverse, would be very much more than counterbalanced by the increased amount of the secretion, but excessive amounts of the bitters may retard digestion.

While a large number of official substances are used as simple bitters or stomachics, it will not be necessary to enumerate more than a few of the more popular to illustrate the variety of this class of drugs.

GENTIANA.—U. S. P.—The dried rhizome and roots of *Gentiana lutea,* constitute by far the best known and the most widely used of all simple bitters. This drug is not alone of interest medicin-

ally, but it has also taken an important part in the folklore, traditions and legends of European peoples. It is said to have been introduced into medicine by Gentius, King of Illyria, who discovered its medicinal virtues.

FLUIDEXTRACTUM GENTIANÆ.—U. S. P.—This is made with diluted alcohol.

Average dose: 1 c.c. (15 minims).

EXTRACTUM GENTIANÆ.—U. S. P.—This is an aqueous extract of gentian evaporated to pilular consistence.

Average dose: 0.25 gm. (4 grains).

TINCTURA GENTIANÆ COMPOSITA.—U. S. P. —This represents 10 per cent. of gentian, 4 per cent. of bitter orange peel and 1 per cent. of cardamom in 60 per cent. alcohol.

Average dose: 4 c.c. (1 fluidram).[1]

CALUMBA.—U. S. P.—The dried root of *Jateorhiza palmata,* was introduced into Europe by the Portuguese in the seventeeth century and has been much employed as a simple bitter since that time, particularly on the continent of Europe.

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1. The compound tincture of gentian is probably the most popular of all stomachics and is widely used either alone or in combination with a mild antacid, such as sodium bicarbonate. A mixture that is largely used, particularly in hospital practice, may be compounded somewhat as follows:

℞.	Tinct. gent. comp.	ʒx	40
	Sodii bicarbonatis	gr. xc	6
	Aquæ q. s. ad	℥iii	100

To be given in doses of 2 or 3 teaspoonfuls before meals.

Such a prescription, of course, may be varied in innumerable ways, the addition of compound tincture of cardamom will not alone improve its appearance, but will also make it much more acceptable, in that it makes the whole mixture more aromatic. The addition of tincture of capsicum, 0.2 c.c. or 0.3 c.c. (3 to 5 minims) to each dose, makes the mixture sharp and pungent and may be desirable, particularly in cases of alcoholic gastritis.

FLUIDEXTRACTUM CALUMBÆ.—U. S. P.—This is made with 70 per cent. alcohol.

Average dose: 2 c.c. (30 minims).

TINCTURA CALUMBÆ.—U. S. P.—This represents 20 per cent. of the crude drug.

Average dose: 4 c.c. (1 fluidram).

QUASSIA.—U. S. P.—The wood of *Picarasma excelsa*—Jamaica quassia or of *Quassia amara*—Surinam quassia, appears to be more popular in England than in this country. The official preparations are:

FLUIDEXTRACTUM QUASSIÆ.—U. S. P.—This is made with 33 per cent. alcohol.

Average dose: 0.5 c.c. (8 minims).

EXTRACTUM QUASSIÆ.—U. S. P.—This is an aqueous extract of quassia, representing ten times its weight of the crude drug.

Average dose: 0.05 gm. (1 grain).

TINCTURA QUASSIÆ.—U. S. P.—This represents 20 per cent. of quassia in 35 per cent. alcohol.

Average dose: 2 c.c. (30 minims).

Two other drugs which are frequently used by American physicians are chirata and berberis.

CHIRATA.—U. S. P.—The dried plant of *Swertia chirayita* is a comparatively recent addition to European medicine, though it has long been used and held in high esteem by the Hindus. The only official preparation in our Pharmacopeia is:

FLUIDEXTRACTUM CHIRATÆ.—U. S. P.—This is made with diluted alcohol.

Average dose: 1 c.c. (15 minims).

BERBERIS.—U. S. P.—(Barberry)—The rhizome and roots of *Berberis aquifolium*.

FLUIDEXTRACTUM BERBERIS.—U. S. P.—This is made with diluted alcohol.

Average dose: 2 c.c. (30 minims).

AROMATICS.

Aromatics contain volatile oils, on which they depend for their flavor and for a slightly irritant action on the mucous membranes. Brandl found that the irritation and the consequent hyperemia of the mucous membrane of the alimentary canal, due to sharp tasting substances, caused increased absorption of certain products of digestion. As the aromatics usually have an agreeable taste, they probably increase gastric secretion by reflex stimulation, but it has not been demonstrated that they increase the amount of hydrochloric acid or of the digestive ferments.

All volatile oils have an antiferment action, and the aromatics, therefore, may lessen gastric fermentation.

The slightly irritant effect, with the hyperemia, must be the main factors in their effects on digestion after that of reflex stimulation.

In this connection it is to be remembered that nausea, pain in the stomach and other symptoms of functional disturbances of the gastrointestinal canal are often promptly relieved by external application of heat or even by a mustard footbath, which can only act reflexly.

It is easy to understand why pure air and interesting surroundings play such an important rôle in appetite and digestion when we consider how completely those functions are under the control of the reflexes, mere change of location being much less important than the substitution of interesting,

for monotonous, surroundings, and in advising change of scene with outdoor life these details can not be too carefully considered.

The official aromatic bitters include:

CALAMUS.—U. S. P.—(Sweet Flag).—The dried rhizome of *Acorus calamus* was known to the ancients and is still largely used in Europe, though not so popular in this country.

FLUIDEXTRACTUM CALAMI.—U. S. P.—This is made with 75 per cent. alcohol.

Average dose: 1 c.c. (15 minims).

AURANTII AMARI CORTEX.—U. S. P. (Bitter Orange Peel).—The dried rind of the unripe fruit of *Citrus vulgaris* has long been used as an aromatic bitter, but is chiefly used as an addition to other drugs, as in the compound tincture of gentian and the compound tincture of cinchona.

FLUIDEXTRACTUM AURANTII AMARI.—U. S. P. —This is made with 65 per cent. alcohol.

Average dose: 1 c.c. (15 minims).

TINCTURA AURANTII AMARI.—U. S. P.—This represents 20 per cent. of the crude drug and contains 60 parts of alcohol.

Average dose: 4 c.c. (1 fluidram).

ASTRINGENT BITTERS.

Drugs that might properly be classed as astringent bitters are numerous, and, therefore, we shall enumerate but a few of the more important.

CIMICIFUGA. U. S. P. The dried rhizome and roots of *Cimicifuga racemosa*, a plant that is a native of North America, have been used extensively in some sections of the United States.

FLUIDEXTRACTUM CIMICIFUGÆ.—U. S. P.—This is made with strong alcohol.

Average dose: 1 c.c. (15 minims).

TINCTURA CIMICIFUGÆ.—U. S. P.—This is made with alcohol.

Average dose: 4 c.c. (1 fluidram).

SERPENTARIA.—U. S. P.—The rhizome and roots of *Aristolochia serpentaria,* popularly known as Virginia snakeroot, have been used in Europe for over 200 years.

FLUIDEXTRACTUM SERPENTARIÆ.—U. S. P.—This is made with 80 per cent. alcohol.

Average dose: 2 c.c. (30 minims).

TINCTURA SERPENTARIÆ.—U. S. P.—This represents 20 per cent. of the crude drug and is made with a menstruum containing 65 parts of alcohol.

Average dose: 4 c.c. (1 fluidram).

HYDRASTIS.—U. S. P.—The rhizome and rootlets of *Hydrastis canadensis*, a perennial plant that is indigenous to Canada and the United States east of the Mississippi River.

FLUIDEXTRACTUM HYDRASTIS.—U. S. P.—This is made with a menstruum containing 60 parts of alcohol, with glycerin and water, and should contain not less than 2 per cent. of hydrastin.

Average dose: 2 c.c. (30 minims).

TINCTURA HYDRASTIS.—U. S. P.—This represents 20 per cent. of the crude drug and is made with 65 per cent. alcohol.

Average dose: 4 c.c. (1 fluidram).

CINCHONA.—U. S. P.—While undoubtedly better known and more extensively used as a bitter stomachic than any of the preceding, it is unnecessary to recount the origin or the uses of this drug.

It is official under two titles: Cinchona and Cinchona Rubra. Of the former we have:

FLUIDEXTRACTUM CINCHONÆ.—U. S. P.—This is made with 80 per cent. alcohol and contains 4 per cent. of the ether-soluble alkaloids of cinchona.

Average dose: 1 c.c. (15 minims).

TINCTURA CINCHONÆ.—U. S. P.—This represents 20 per cent. of the crude drug and should contain 0.75 per cent. of cinchona alkaloids.

Average dose: 4 c.c. (1 fluidram).

The only official preparation of red cinchona is the old, and still popular, Huxham's tincture of bark.

TINCTURA CINCHONÆ COMPOSITA.—U. S. P.—This represents 10 per cent. of red cinchona, 8 per cent. of bitter orange peel and 2 per cent. of serpentaria.

Average dose: 4 c.c. (1 fluidram).

NUX VOMICA.—U. S. P.—The dried ripe seed of *Strychnos nux vomica,* although not containing sufficient tannin to be classed as an astringent bitter, forms an inky mixture when iron is added to it. It is frequently used as a bitter stomachic. The available preparations are:

FLUIDEXTRACTUM NUCIS VOMICÆ.—U. S. P.—This contains 1 per cent. of strychnin.

Average dose: 0.05 c.c. (1 minim).

TINCTURA NUCIS VOMICÆ.—U. S. P.—This contains 2 per cent. of extract of nux vomica and is assayed to contain 0.1 per cent. of strychnin.

Average dose: 0.6 c.c. (10 minims).

Bitters, and more particularly the aromatic bitters, are indicated in loss of appetite when it is not due to grave gastric disturbances. When catarrh

of the gastric mucous membrane complicates the condition, an astringent bitter, such as serpentaria, cimicifuga or cinchona, should be used. In the absence of catarrh, indigestion accompanied by insufficient gastric secretion, may be treated with a simple bitter, such as gentian or calumba, which may be used alone, but it is very much more often advisable to combine the simple bitters with aromatics.

The individual taste of the patient should always be considered in the choice of the aromatic. Men often like simple bitters, such as gentian or gentian and orange, a fact attested by the extraordinary popularity a few years ago of a certain bitters, which consisted practically of compound tincture of gentian. Women usually prefer mildly aromatic and not very bitter substances, while children are generally averse to them altogether.

When excess of acidity exists bitter substances will probably increase the trouble. Just as bitters and aromatics produce a greater effect in cases of functional disturbances, so iron is useful in anemia, though it has little influence in health, and it is often found advisable to combine iron with bitters, in which case the astringents are to be avoided because of the chemic reaction, whereby an inky mixture is formed, disagreeable alike to sight and taste—two great objections in this class of remedies.

Many bitters which are not usually classed as astringents contain enough tannin or similarly acting substances to give inky mixtures with ferric salts; such, for instance, are gentian and nux vomica. Calumba, therefore, is to be given the

preference in all cases in which a bitter is to be combined with a soluble salt of iron. Detannated preparations of cinchona and even solutions of the cinchona alkaloids have little to recommend them in preference to calumba as a simple bitter.

The following illustrates the combination of a simple bitter with iron:

℞.	Tinct. calumbæ	℥iii	100
	Tinct. ferri chloridi	m. lxxv	5
	Aquæ q. s. ad	℥vi	200

M. Sig.: A tablespoonful may be given half an hour before meals to men, while a teaspoonful will usually suffice for women.[2]

The possible combinations of aromatic bitters are infinite, and, as previously stated, the individual taste is to be considered rather than slavish adherence to any one formula.

For an astringent bitter the fluid extract or the tincture of cinchona, cimicifuga or serpentaria may be combined somewhat as follows:

℞.	Fluidextract cinchonæ		
	Tinct. gentianæ comp., āā	ʒxii	50

M. Sig.: One teaspoonful to be given before meals.

For women it will be well to increase the amount of aromatics, in which case the compound tincture of cardamom may be substituted for the compound tincture of gentian and the mixture even further diluted with aromatic elixir, if thought desirable, as follows:

℞.	Fluid extract. cinchonæ	ʒv	20
	Tinct. cardamomi comp.		
	Elixir aromatici, āā	ʒx	40

M. Sig.: One teaspoonful of this mixture with water, to be given before meals.

[2] While small doses of iron well diluted may be given with bitters before meals, if larger doses are given after eating they are borne better than they would be if given on an empty stomach.

A mixture of nux vomica and sodium bicarbonate offers a number of advantages as an efficient and comparatively harmless stomachic. It is made as follows:

℞. Tinct. nucis vom.....m. lxxv	5	
Sodii bicarb.....gr. cl	10	
Aquæ dest q. s. ad.....℥v	150	

Although technically this formula involves an incompatibility—sodium bicarbonate and the alkaloids of nux vomica—practically it is very satisfactory indeed. If the mixture is filtered and allowed to stand for 24 hours before being dispensed it will be found to have developed a very pleasant ethereal odor that adds materially to its effectiveness. The usual dose for adults is one tablespoonful before meals. For a patient with chronic constipation the addition of 1 or 2 c.c. (15 to 30 minims) of the fluidextract of cascara sagrada will be found to be highly satisfactory. One argument in favor of this combination is that it contains little alcohol—virtually none.

CARMINATIVES.

The origin of this word is in doubt, some authorities maintaining that it comes from *carmen,* a charm, and the term is even now used somewhat loosely for those agents which produce a sense of warmth and well-being and which act as antispasmodics, or which expel gases from the gastrointestinal canal. When given with cathartics they lessen the griping pain of these drugs, and, being antiseptic, they inhibit the formation of gas by fermentation.

According to the accepted definition a greater or less number of substances can be included in this

particular class. The official carminatives afford a very wide range of choice, as they include practically all aromatic bitters, nearly all the aromatic volatile oils, besides such substances as ginger and capsicum, which contain pungent resinous constituents, alcohol, ether, chloroform and many other agents which produce a sense of warmth when swallowed.

Carminatives are among the most ancient of remedies and are indicated in pain in the stomach or bowels when due to simple indigestion or distension by gas, but not when there is inflammation; in the latter case—for instance, in appendicitis or in peritonitis—carminatives are apt to augment the trouble.

Many of these substances are well known as household remedies and it will suffice to enumerate only the more important ones.

ZINGIBER.—U. S. P.—Ginger has been used from time immemorial in eastern Asia; it was well known to the ancient Greeks, and is even now, perhaps, the most popular of all the carminatives. The most widely used of the official preparations is the tincture.

TINCTURA ZINGIBERIS.—U. S. P.—This represents 20 per cent. of the crude drug exhausted with alcohol.

Average dose: 2 c.c. (30 minims).

FLUIDEXTRACTUM ZINGIBERIS.—U. S. P.—This is an alcoholic extract.

Average dose: 1 c.c. (15 minims).

OLEORESINA ZINGIBERIS.—U. S. P.—This is now prepared by means of acetone.

Average dose: 0.03 gm. (½ grain).

Half a teaspoonful of the tincture may be given in a little hot water or with sugar.

The oleoresin is much more active, and a drop of it may be thoroughly well mixed with powdered sugar and from one-eighth to one-fourth of the quantity given to a child, but not to an infant. It may also be added in half-drop doses or less to bulky cathartic pills or mixtures, but in either case it should be well diluted.

While ginger is very commonly used alone as just mentioned, it may be prescribed somewhat as follows:

℞.	Tinct. zingiberis	ʒiv	16
	Chloroformi	ʒi	4
	Elixir aromat. q. s. ad	℥iii	100

M. Sig.: One teaspoonful thirty minutes after eating.

CAPSICUM.—U. S. P.—Capsicum has been in use as a condiment, in eastern countries, from a very early period. It is intensely pungent and is particularly useful in cases of alcoholic gastritis.

Average dose: 0.05 gm. (1 grain).

TINCTURA CAPSICI.—U. S. P.—Tincture of Capsicum represents 10 per cent. of the drug in 90 per cent. alcohol.

Average dose: 0.5 c.c. (8 minims).

FLUIDEXTRACTUM CAPSICI.—U. S. P.—Fluidextract of capsicum is directed to be made with strong alcohol.

Average dose: 0.05 c.c. (1 minim).

OLEORESINA CAPSICI.—U. S. P.—Is directed to be made by using acetone as the solvent.

Average dose: 0.030 gm. (30 mg. ½ grain).

THE OFFICIAL MINTS.

Of the large number of aromatic drugs of the mint family, two have attained more than ordinary popularity as carminatives. The revisers of the Pharmacopeia have, indeed, been impartial in their description of these two substances and have treated them absolutely alike, so that from their status as official drugs it would be difficult to say whether peppermint or spearmint should be accorded the preference. It will be safe to assert, however, that peppermint is the more widely used. It is official as:

MENTHA PIPERITA.—U. S. P. (Peppermint).—The dry leaves and flowering tops.

Average dose: 4 gm. (1 dram). This is sometimes used in infusion.

OLEUM MENTHÆ PIPERITÆ.—U. S. P.—This is a volatile oil distilled from the fresh and partly dried leaves and flowering tops of peppermint.

SPIRITUS MENTHÆ PIPERITÆ.—U. S. P.—This is an alcoholic solution of 10 parts of oil of peppermint filtered through 1 part of bruised peppermint, which imparts to it a distinct greenish color.

Average dose: 2 c.c. (30 minims).

AQUA MENTHÆ PIPERITÆ.—U. S. P.—This is a saturated aqueous solution of oil of peppermint.

Average dose: 15 c.c. (4 fluidrams).

As above noted, spearmint, *Mentha viridis,* is official under corresponding headings and the doses are, of course, the same.

The uses of these official mints are too numerous and too well known to require description in detail. They appear to be particularly useful in gastric fermentation, for which purpose they are usually

given in connection with a mild alkali, like sodium bicarbonate, preferably in the well-known mixture of soda mint of the National Formulary or the widely used soda-mint tablets.[3]

Accumulations of gas in the stomach which prove most distressing can often be promptly relieved by administration of 20 grains of sodium bicarbonate or potassium bicarbonate dissolved, preferably in hot water, to which from 10 to 20 drops of spirit of peppermint or spearmint may be added.

ASAFETIDA.

ASAFŒTIDA.—U. S. P.—A gum resin obtained from the root of one or more species of *Ferula,* was held in high esteem by the ancient Greek physicians and has been in general use since that time.

Average dose: 0.25 gm. (4 grains).

PILULÆ ASAFŒTIDÆ.—U. S. P.—Each pill contains 0.2 gm. (3 grains) of asafetida and 0.06 gm. (1 grain) of soap.

Average dose: 2 pills.

TINCTURA ASAFŒTIDÆ.—U. S. P.—This represents 20 per cent. of asafetida in alcohol.

Average dose: 1 c.c. (15 minims).

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3. The Mistura Sodæ et Menthæ of the National Formulary consists of:

Sodium bicarbonate	grs. lxxv	5
Aromatic spirit of ammonia	m. xv	1
Spearmint water to make	℥iii	100

Mix and filter.

The average dose of this preparation is from 2 to 3 teaspoonfuls.

Soda mint tablets as furnished by manufacturers usually consist of 0.3 gm. (5 grains) of sodium bicarbonate with 0.002 (1/30 minim) of oil of peppermint.

EMULSUM ASAFŒTIDÆ.—U. S. P.—This represents 4 per cent. of asafetida in water.

Average dose: 15 c.c. (4 fluidrams).

As an addition to other carminatives, asafetida in substance was at one time very popular. At present it is not often administered in any form other than suppositories. These are largely used after surgical operations to overcome the atony and partial paralysis that frequently accompanies surgical interference in the abdomen.

The emulsion is used extensively, as a clyster, to relieve accumulations of gas in the intestines, after abdominal operations. It was at one time a very popular remedy for colic in infants, but the nauseous taste makes it very disagreeable and the greater number of infantile complaints, in which it might be indicated, are much more effectively treated with a laxative such as castor oil or magnesia, and by the application of warmth to the abdomen.

The National Formulary contains a number of carminative mixtures. Among the better known are: Mistura Carminativa, or Dalby's Carminative, containing about three drops of tincture of opium in the ordinary teaspoonful; Mistura Chloroformi et Cannabis Indicæ Composita, which, in addition to Cannabis Indica, contains one and one-eighth grains of morphin sulphate to the fluid ounce, chloroform, ether and other ingredients. It is difficult to see wherein these are superior to the worst type of nostrums, and it is unfortunate that they should be included in a work that has official recognition.

The habitual use of these and such preparations as Mrs. Winslow's Soothing Syrup, Chamberlain's

Colic, Cholera and Diarrhea Remedy, Kopp's Baby's Friend[4] and others which have been exposed in THE JOURNAL, can not be too strongly condemned. If an opiate is thought to be necessary, it is much better to advise the nurse or mother to give five drops or more of paregoric, with warnings about the disadvantages and the dangers of its indiscriminate use.

CHLOROFORM AND ETHER.

CHLOROFORMUM.—U. S. P.—As a carminative, chloroform probably deserves a much more extended use than it now has.

Average dose: 0.3 c.c. (5 minims). This may be given either on sugar, in shaved ice, or in ice-cold water.

SPIRITUS CHLOROFORMI.—U. S. P.—This contains 6 per cent. of chloroform in alcohol.

Average dose: 2 c.c. (30 minims).

EMULSUM CHLOROFORMI.—U. S. P.—This contains 4 per cent. of chloroform with a small proportion of expressed oil of almonds, emulsified with tragacanth.

Average dose: 8 c.c. (2 fluidrams).

AQUA CHLOROFORMI.—U. S. P.—This is a saturated solution containing about one-fifth of a minim to the teaspoonful.

Average dose: 16 c.c. (4 fluidrams).

ÆTHER.—U. S. P.—Ether, "sulphuric ether" of the early pharmacopeias, has long been in use as a carminative.

Average dose: 1 c.c. (15 minims).

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4. See THE JOURNAL A. M. A., vol, xliv, p. 666.

SPIRITUS ÆTHERIS.—U. S. P.—This contains about 33 per cent. of ether.

Average dose: 4 c.c. (1 fluidram).

SPIRITUS ÆTHERIS COMPOSITUS.—U. S. P.—The well-known and widely-used Hoffman's anodyne contains, in addition to ether, about 2.5 per cent. of ethereal oil.

Average dose: 4 c.c. (1 fluidram).

Compound spirit of ether, in addition to its other uses, has long enjoyed a special reputation in hysteria due to gastric disturbances. It is disagreeable to the taste, however, and probably possesses no advantage over hot whisky and water, or spirit of nitrous ether.

The spirit of chloroform, diluted with aromatic elixir, or the emulsion of chloroform given alone, promptly affords a sense of warmth in the stomach and will usually give relief in cases of colic and pain.

Chloroform may be prescribed as follows as a carminative:

℞.	Tinct. capsici	ʒiii	12
	Spiritus camphoræ	ʒiii	12
	Chloroformi	ʒi	4
	Alcohol diluti q. s. ad	℥iii	100

M. Sig.: Half a teaspoonful as a dose.

Alcoholic liquids in general are often useful, but their use and their numerous disadvantages can not be advantageously discussed in this connection.

CLOVES AND OTHER AROMATIC SUBSTANCES.

CARYOPHYLLUS.—U. S. P.—(Cloves.)—The dried flower buds of *Eugenia aromatica*. This remedy appears to have been known to the early Egyptians, but was not known to the later Greeks. In

Europe this drug, probably introduced by the Arabians, has been known for centuries.

Average dose: 0.25 gm. (4 grains).

OLEUM CARYOPHYLLI.—U. S. P.—This is a volatile oil distilled from cloves.

Average dose: 0.05 c.c. (1 minim).

The oil of cloves is much more frequently used for its anesthetic and caustic effect on exposed nerves in carious teeth than as a carminative, but it may be used for the latter purpose, in which case it is better to add it to spirit of peppermint or some other alcoholic carminative preparations before diluting with water.

Oil of cinnamon resembles oil of cloves in its carminative effect, and the official tincture of cinnamon is also useful for the same purpose, but is more commonly employed as an adjuvant or flavor for other more active carminative agents, and in diarrhea.

Mustard, pepper and nutmeg are not used medicinally as carminatives, but are much employed as condiments to serve practically the same purpose.

CHAPTER VII.

DIGESTANTS AND DIETETICS.

The digestive ferments are of only minor importance in therapeutics, and most often they are entirely useless. We know but little of the conditions demanding their use, and in the great majority of cases of indigestion there is no lack of these enzymes in the alimentary canal.

The general subject of dietetics presents a very great number of difficulties even to the most skilful specialist. Frederich Müller closed a series of lectures on "the pathology of digestion" with the remark that there were few subjects in medicine on which he would be so loath to write a book as on that of dietetics.

In view of this attitude the title of this chapter is almost a misnomer, for it is our purpose to call attention to some of the abuses which obtain in connection with these substances rather than attempt to give extended information for the use of the digestive ferments and the predigested foods. The general subject of nutrition, on the other hand, is so extensive that it can be touched on only very briefly.

It has been shown repeatedly that where several of the digestive ferments are contained in a mixture one or the other of them is rapidly destroyed.

The actions which mainly concern us may be stated briefly as follows: Dilute hydrochloric acid and gastric juice destroy trypsin (pancreatin) and

diastase or ptyalin in a few hours, the rate depending on the degree of acidity.

Hydrochloric acid and pepsin act much more energetically in destroying these ferments.

Alkalies alone destroy pepsin, and alkalies plus trypsin destroy pepsin very much more rapidly. As Sollmann has put it, it is as absurd to expect the simultaneous action of pepsin and trypsin or pancreatin as to expect the simultaneous action of an acid and an alkali from a mixture of the two.

Alcohol and numerous other antiseptics slowly destroy pepsin so that ready-made preparations are of necessity variable and very commonly inert.

The better class of manufacturers claim that they make preparations containing pepsin with pancreatin only in response to a demand. This is not wholly true, however, for every text-book worthy of note which deals with the subject at all states distinctly that pepsin and pancreatin are incompatible, that pepsin acts only in an acid medium in which it destroys pancreatin, and that pancreatin destroys pepsin in a neutral or alkaline mixture. No writer worthy of attention at present pretends that pepsin and pancreatin are useful in combination, and it is not reasonable to suppose that a disreputable firm, making false claims, would create so great a demand for a rival's goods that the rival would be compelled to put out a mixture known to be worthless.

It is difficult to understand how any reasonably careful physician can read the evidence on this subject given in THE JOURNAL of the American Medical Association (Feb. 2, 9 and 16, 1907), including the article by Sollmann, and continue to

prescribe these substances in combination, or even singly, except in rare cases.

The ptyalin of the saliva acts on starchy foods, converting them into dextrin and maltose and finally into glucose. When the food is thoroughly masticated, and thus insalivated, the action of the ptyalin may continue in the interior of the food masses in the stomach, since the gastric juice acts mainly on the external surfaces and, therefore, does not come at once into contact with all of the contained ptyalin.

Starchy foods, such as gruel, may be partially digested by the addition of diastase (from grain) before being taken, but it is wholly useless to take diastase in solution, since, as already stated, it would be inhibited by the hydrochloric acid and destroyed by the pepsin before it could exert any important action on the food, because it is not then protected by being enclosed in masses of food.

It is evidently irrational to give pepsin unless there is some reason to suppose that there is a deficiency of that enzyme in the gastric juice, and then it should be given in powder or only in freshly made solutions, unless the glycerin extract is used.

The practice of giving pepsin, or even a mixture of the digestive enzymes in every case of indigestion, regardless of whether proteids, carbohydrates or fats are the disturbing factors, is as irrational as would be the practice of trying to cure every disease of which fever is a symptom by the use of one of the coal tar antipyretics.

The only conceivable method of giving pan-

creatin with benefit consists in protecting it from solution in the stomach, by coating with keratin or salol, or by administering it toward the close of gastric digestion, in alkaline solution, when it would probably pass fairly rapidly into the intestine, but it could exert only a minor influence under the latter circumstances.

Hydrochloric acid is much more frequently wanting than is pepsin or trypsin and it is sometimes useful to administer the dilute acid.

Hydrochloric acid is not a proprietary article, however, and there are no financial interests to be served by recommending its use. It has been suggested that much larger doses than those commonly given may be required, but Osler does not advise very large amounts.

It is quite needless to mention the various proprietary preparations by name which have been exploited with so little credit to the medical profession and with such large financial returns to their manufacturers, for every intelligent physician can supply a liberal number of these names for himself, and it can not be too plainly stated that all alcoholic preparations of digestive enzymes, whatever the alcohol content may be, are variable or inert, and that all mixtures of the various digestive enzymes are as absurd as mixtures of acids and alkalies, where the action of the resulting salt is not desired, or as it would be to attempt to apply heat and cold simultaneously by putting hot water and ice in an ice cap.

It is very much more rational to assist the digestion by dainty appetizing dishes and pleasing

surroundings than to administer digestive ferments.[1]

While rennin, occurring in the gastric juice, curdles milk, its precise use in digestion is not known; in a practical way it is used to prepare curds and whey and is of considerable importance in the diet kitchen.

Trypsin has been suggested as a cure for cancer and has been noisily praised as such in the public press; it is as yet quite impossible to say whether it possesses really curative value or not. It may be recalled, however, that it was just as noisily proclaimed, some years ago, for the removal of the diphtheritic membrane.

The vegetable pepsin, so called, papayotin, which is said to act in acid, alkaline or neutral media, has not proved to be of any distinct value, and this is only what was to be expected in view of the fact that the fault probably seldom lies in the want of secretion of the digestive enzymes.

Hydrolysis or digestion of proteids may also be accomplished by means of mineral acids or superheated steam, and it is reported that the resulting artificial peptones and albumoses have been offered as foods. Whatever may be said of the value of the predigested foods as a class, it must be admitted that the best of them are of little actual value, and there is considerable evidence to indicate that when prepared, by means of mineral acids

1. That sufficient attention is not paid to this may be shown by the experience of one of the authors in one of the larger hospitals of New York. While convalescent from typhoid fever he was given ice cream and other food with a dirty piece of rubber adhesive plaster attached to every spoon and article of tableware (except such as he had brought from home), and some surprise was expressed that he ate almost nothing while in the hospital.

or steam, the resulting peptones do not act as food. Predigested foods should at least be obtained by the action of the digestive enzymes.

OFFICIAL PREPARATIONS.

PEPSINUM.—U. S. P.—Pepsinum is described as a proteolytic ferment or enzyme, derived from the glandular layer of the fresh stomach of the hog. When assayed according to the process described in the Pharmacopeia, pepsin should be capable of digesting no less than 3,000 times its own weight of freshly coagulated and disintegrated egg albumin.

Pepsin is soluble in about 50 parts of water, but is insoluble in alcohol. It is incompatible with alkalies, alcohol, many of the salts of the heavy metals and strong mineral acids; even the presence of more than 0.5 per cent. of hydrochloric acid rapidly destroys its proteolytic activity.

Average dose: 0.25 gms. (4 grains).

PANCREATINUM.—U. S. P.—Pancreatin is a mixture of enzymes naturally existing in the pancreas of warm-blooded animals. The commercial article is usually obtained from the pancreas of the hog or the ox. It is officially described as consisting principally of amylopsin, myopsin, trypsin and steapsin, and when assayed by the process given in the Pharmacopeia should be capable of converting no less than 25 times its own weight of starch into substances soluble in water.

Pancreatin is slowly, but not completely, soluble in water; it is insoluble in alcohol and is incompatible with pepsin and mineral acids.

Average dose: 0.50 gm. (8 grains).

EXTRACTUM MALTI. — U. S. P. — Extract of malt, as now official, has the consistency of thick honey and possesses amylolytic properties.

It is frequently used as a vehicle for other substances.

Average dose: 16 c.c. (4 fluidrams).

NATIONAL FORMULARY PREPARATIONS.

The abuse and the general uselessness of many of the combinations of digestive ferments is well illustrated by the preparations that are included in the recent, third, edition of the National Formulary. No less than 18 preparations, many of them involving well known chemical incompatibilities, are included. We may enumerate:

ELIXIR PEPSINI, BISMUTHI ET STRYCHNINÆ.—N. F.

ELIXIR PEPSINI ET BISMUTHI.—N. F.

ELIXIR PEPSINI ET FERRI.—N. F.

ELIXIR CINCHONÆ, FERRI ET PEPSINI.—N. F.

ELIXIR CINCHONÆ, PEPSINI ET STRYCHNINÆ.—N. F.

GLYCERITUM PEPSINI.—N. F.

LIQUOR PEPSINI.—N. F.

LIQUOR PEPSINI AROMATICUS.—N. F.

LIQUOR PANCREATICUS.—N. F.

PULVIS PEPSINI COMPOSITUS.—N. F.

PEPSINUM SACCHARATUM.—N. F.

Among the more widely used preparations we have:

ELIXIR DIGESTIVUM. N. F. Compound digestive elixir represents a mixture of pepsin, pancreatin and diastase with hydrochloric and lactic acids, dissolved in a mixture of glycerin, com-

pound tincture of cardamom and aromatic elixir, colored red with tincture of cudbear.

While this preparation is generally recognized as being inert, so far as digestive properties are concerned, it is nevertheless widely used, chiefly as a vehicle. It is perhaps needless to add that because of the absurdities involved its future use should be discouraged, and it is to be hoped that future revisions of the National Formulary will present in its stead a less objectionable red elixir.

Average dose: 8 c.c. (2 fluidrams).

ESSENTIA PEPSINI.—N. F.—Essence of pepsin represents a mixture of pepsin, rennin and a small amount of lactic acid in an aromatic vehicle containing glycerin and wine. In common with the numerous proprietary preparations of a similar nature now on the market, it is essentially a rennin preparation and has its chief uses in the making of junket, curds and whey, as described below. It is also popular as a vehicle for iodids and bromids, though these, in turn, tend to destroy the contained pepsin.

Average dose: 8 c.c. (2 fluidrams).

PULVIS PANCREATICUS COMPOSITUS.—N. F.—Peptonizing powder consists of a mixture of two parts of pancreatin and eight parts of sodium bicarbonate. It is used in the preparation of peptonized milk and in the making of:

PULVIS PRO LACTE HUMANISATO.—N. F.—Milk powder, or humanized milk powder, represents a mixture of 35 parts of compound pancreatic powder N. F. and 965 parts of sugar of milk. This preparation is designed for use in preparing humanized milk.

Humanized milk. The directions for this preparation, as given in the National Formulary, are as follows:

Triturate 6.5 gms. (100 grains, or about a heaping teaspoonful) of the humanizing powder with 60 c.c. (2 fluidounces or about 4 tablespoonfuls) of water and transfer the mixture to a clean bottle containing 60 c.c. (2 fluidounces or about 4 tablespoonfuls) of fresh cows' milk and 15 c.c. (½ fluidounce or about 1 tablespoonful) of fresh sweet cream. Mix thoroughly and immerse the bottle in water heated to 38° C. (100° F.) for 15 minutes, then pour the mixture into a suitable vessel and heat it quickly to boiling and then immediately allow it to cool to the body temperature.

Humanized milk should be prepared immediately before use and the above directions should be closely followed. If digestion is too prolonged the resulting milk will be bitter and unpalatable. For this reason it is necessary to heat the milk to boiling at the end of the required time for digesting the same.

The milk, and also the cream, should be fresh and sweet and quite free from preservatives of all kinds.

LIQUOR SERIPARUS.—N. F.—Liquid rennet is directed to be prepared from fresh calves' rennet and represents approximately about 10 per cent of the rennet.

This preparation may be used in the making of junket, curds and whey. Where it is to be used merely for curdling the milk without separating the whey as a distinct layer it should be added to the milk previously warmed to a temperature of

about 35° C. (95° F.) but not exceeding 40° C. (104 F.). One part of liquid rennet should coagulate between 200 and 300 parts of cows' milk so that the average direction would be to use half a teaspoonful to 500 c.c. (1 pint) of milk.

Junket and whey may also be prepared by using, in place of the liquid rennet, the essence of pepsin N. F. This preparation contains rennin, and the manufacturers of corresponding proprietary preparations advocate the use of their particular products because the contained pepsin tends to supply the proteid matter contained in milk, in a partially digested form. While this is of doubtful advantage, at best, the claim is misleading unless the preparation is comparatively fresh; the contained rennin has been found to retain its activity for a considerable length of time and the preparation may be used in place of the liquid rennet, in quantities from four to five times greater.

Peptonized milk may be prepared by adding 1.5 gms. (25 grains) of compound pancreatic powder N. F. to 125 c.c. (4 fluidounces) of tepid water contained in a suitable flask or bottle, and afterward add 500 c.c. (1 pint) of fresh cows' milk, previously heated to 38° (100° F.). Maintain the heat at this temperature for thirty minutes, then transfer the container to a cool place.

Peptonized milk, prepared in this way, should not be used when it has been kept over twenty-four hours, or when it has developed a very bitter taste.

The above general process for peptonized milk may be varied in a number of ways, and the degree of digestion may be regulated at will by lengthen-

ing or shortening the time during which the mixture is kept warm. It should be remembered, too, that digestion takes place even at low temperatures and a cold process for peptonizing milk is sometimes recommended. This consists simply of mixing the ingredients enumerated in a clean saucepan or a suitable flask or bottle and placing the same on ice without subjecting it to the warming process.

Partially peptonized milk may be prepared by placing the mixture of peptonizing powder, water and milk, in a clean saucepan or suitable flask or bottle and gradually heating on a water bath until the mixture boils. Then remove and allow to cool, or the milk thus prepared may be given while still warm. The final boiling destroys the ferment and milk thus prepared will not undergo further peptonization on standing.

Peptonized milk may be served with cereals, or in the form of jellies flavored with fruit juices or other desired flavoring. Where its use must be continued for a long period of time it may at times be made more acceptable by mixing with equal portions of aëreated water, or by the addition of an alcoholic beverage with or without spices, such as freshly grated nutmeg.

The simplest form of partially predigested food is toasted bread. Heat converts some of the starch into dextrin (brown color) and by making the bread more brittle favors insalivation. Burning should be avoided, as it not only renders the toast less pleasant to the taste but the carbonized particles are wholly indigestible and may prove irritating to the stomach and intestines.

DIETETICS.

Infant feeding presents a great many problems which can only be discussed with profit by specialists, but there are certain simple facts in dietetics with which the physician should be more familiar than he is now and which require but little thought and study. Infant starvation is not at all uncommon, and many physicians are utterly unable to compute the food requirements of the infant (or adult) and the food values of various foodstuffs. These are exceedingly simple in ordinary cases, in contradistinction to the extreme difficulty of the subject of infant feeding and dietetics in abnormal conditions.

Food values or the energy values of food are commonly expressed in calories (from the Latin, Calor, heat), a calory being that amount of heat which is required to raise the temperature of a liter of water one degree centigrade.

An infant under 3 months requires about 100 calories per day for every kilogram of body weight (about 45 calories per pound). The proportionate requirement diminishes, and between the ages of 3 and 6 months the requirement is 90 calories per kilogram (40 calories per pound), and between 6 months and 1 year 80 calories per kilogram (36 calories per pound), and thereafter about 70 calories per kilogram (30 calories per pound).

It is merely necessary to weigh the child and multiply the weight in kilograms or pounds by the requirement in calories to ascertain the food value needed in any case.

This food value requirement is also, to an extent at least, dependent on the surface area of the

body, hence unusually large children will require somewhat less food per pound than will small ones, or, in other words, the food value per pound of a large child of 6 months will approximate that of a small child of a year.

Having ascertained the weight and energy required in a given case, it is easy to compute the calorific value of the food ingested by multiplying the weight of the carbohydrates and proteids (starches, sugars and albumin) in grams by 4, and the weight of the fats (butter in cream) by 9 to ascertain approximately the number of calories represented.

One ounce avoirdupois may be taken as 30 grams roughly (28, more accurately), and an ounce of sugar represents about 120 calories, while an ounce of butter represents about 250 calories, an ordinary egg about 75 calories, a pint of average good cows' milk represents about 350 calories, mothers' milk somewhat less. The actual value should be determined by examination in any case where it seems probable that a breast-fed infant does not get sufficient nourishment.

Adults require less food per pound of body weight than do infants, and in the case of adults the requirements vary from 25 calories per kilogram (12 calories per pound) during rest in bed (without fever) to 50 or 60 calories per kilogram (22 to 27 calories per pound) during hard labor. Increased activity in the adult does not demand a proportionate increase in the proteid of the diet, if enough carbohydrates and fats are taken, but proteid may supply the increased demand.

During convalescence, when flesh is being added to the body, more proteid is required than is needed by a healthy person of the same weight.

It should be remembered that the food value of such vegetables as celery, tomatoes, lettuce and cabbage is wholly negligible, so far as calorific values are concerned, also that potatoes and rice, as they appear on the table, represent probably not more than 20 per cent. of starch. Sugar, however, is pure carbohydrate except for a wholly negligible amount of moisture.

The commercial liquid predigested foods possess no practical food value. It has been shown that when predigested proteids are given in amounts sufficient to have any practical value their tendency to cause diarrhea interferes with their use, and, furthermore, a person would be kept in a state of continued intoxication by the alcohol contained in much less of the artificial food than would be needed for sustaining life, granting that life could be sustained by the use of predigested foods of this kind.

For a comparison of the theoretic food values of a number of these artificial foods, such as panopepton, liquid peptonoids, tonic beef and others, the reader is advised to read the report of the Council on Pharmacy and Chemistry of the American Medical Association (*Jour.* A. M. A., May 11, 1907, page 1612). The figures that are included in this report are really surprising, particularly from an economic point of view, and were it not for the fact that American medical men have paid altogether too little attention to a careful study of the subject of dietetics, the report itself might be

held to be evidence of our absolute carelessness as medical men.

The table that is embodied in the report includes data obtained from a careful study of eighteen samples of medicinal foods made by ten different manufacturers.

The calories, as proteids and carbohydrates, contained in 500 grams varied from 54.7 to 397.5, while the approximate cost of this quantity varied from $1.00 to $1.54 as compared with milk costing approximately 5 cents and containing upward of 180 calories of food value in proteids and carbohydrates.

The additional calories of available food value in medicinal foods are embodied in the contained alcohol, while in the cows' milk the additional food values consist of fat in a readily assimilable form. Granting that alcohol has the same food value as fat, the cost per day to supply the minimum number of calories necessary to sustain life would vary from $1.56 to $3.39 for the medicinal foods as compared to 20 cents for cows' milk.

If, however, it were practicable to eliminate the consideration of the alcohol in medicinal foods and of the fat in the milk we would have a cost of from $4.33 to $28.97 for the required calories in medicinal foods as compared to 39.5 cents for the corresponding number of calories, in proteids and carbohydrates, to be found in cows' milk.

In one of these artificial foods the food value of the daily dose, exclusive of alcohol, was found to be less than 10 calories, or about 1/150 of the total amount required by an adult resting in bed. To put it in another way, the total daily dose of this

medicinal food equalled in food value about one-seventh of an egg or an ounce and a half of milk—and yet on such frail reeds are we expected to lean in a crisis.

The value of alcohol as a food has been the subject of a great deal of discussion. It may be said that alcohol may replace carbohydrates or fats, to a very small extent, but it does not lessen in the slightest degree the minimum amount of proteid metabolized, which must be supplied in the food or drawn from the tissues. In other words, if a patient is able to take a bare sufficiency of carbohydrates and fats the addition of alcohol does not diminish the amount of proteid which must be taken to prevent loss of weight.

According to the researches of Chittenden, the minimum proteid requirement for adults is much less than was formerly supposed. He found that 40 grams (1⅓ ounces) of ordinary beef or six eggs (roughly), with carbohydrates sufficed to keep himself, weighing 60 kilograms (130 pounds) in nitrogen equilibrium.

While the minimum requirement is a matter of importance when one wishes to supply the actual needs of the body, it is not often that the diet of healthy adults does not contain an excess of proteid except among the very poor.

Professor Chittenden thinks proteids greatly in excess of the minimum requirements are injurious, but this view is not generally accepted, and some standard dietaries give 150 grams (5 ounces) or more of proteid corresponding to about 600 grams (1¼ pounds) of beef as the daily amount for

a man weighing 70 kilograms (150 pounds) doing hard work.

Standard dietaries show considerable variation, whether it be for prison fare or the ration of the soldier or hospital diet.

Two of these are given in order to afford an approximate idea of the kind and quantity of foods required under different conditions. The amounts in the first table are for a man weighing 70 kilograms (150 pounds) with work varying from light work to hard labor.

Proteid	100 to 150 grams	(3 to 5 ounces)
Fat	46 to 100 grams	(1½ to 3 ounces)
Carbohydrates	375 to 565 grams	(13 to 20 ounces)

The total calories in this list vary from 2,450 to 4,150.

The following table represents approximately the average diets of several hospitals in Germany:

Proteid	100 grams	(3 ounces)
Fat	50 grams	(1½ ounces)
Carbohydrates	150 to 400 grams	(5 to 13 ounces)

Here the calorific values vary from about 1,400 to 2,300.

It should be remembered that ordinary beef or other meat may contain more fat than proteid, but the leanest meat obtainable may be considered as about one-third proteid. An egg contains approximately 6 grams of proteid, while cereals contain little or none.

CHAPTER VIII.

ASTRINGENTS.

Astringents are substances which produce a constriction of all the solid tissues with which they are brought into intimate contact. Substances of this class have a peculiar action on mucous membranes, causing wrinkling of their surfaces and diminution of secretion; they precipitate not only proteids and gelatin, but also alkaloids and many glucosids.

The action of astringents, irritants and caustics is largely a matter of degree, the caustics acting as astringents when sufficiently diluted, while all astringents produce at least a transient and slight irritation, and when applied in concentrated form to mucous membranes many of those classed as mere astringents are capable of causing considerable irritation, which in the stomach may give rise to vomiting, and in the intestine to diarrhea. Some astringents are essentially mild in their action, while others, being nearly insoluble, can not be brought into intimate contact with the tissues in concentrated form; these can not produce more than a very mild and fleeting irritation, or stimulation, which is followed by lessened permeability of the capillary walls and diminished congestion.

By their irritant action, drugs of this particular class may increase a severe acute inflammation without being able to produce their typical astringent effect, hence they are not nearly so useful in such conditions as in chronic inflammations.

The vegetable astringents owe their action mainly to the presence of tannins, substances belonging to an ill-defined group, possessing an astringent action as their best defined property. Other organic acids play only a minor rôle as astringents. The tannins give blue-black or greenish-black reactions with ferric salts; they precipitate proteids (leather being the product formed with connective tissue), alkaloids, metals and some other substances; they yield pyrocatechin or pyrogallol on destructive distillation. Their therapeutic actions are independent of their chemical peculiarities, and they are severally indicated rather with reference to the presence or absence of extractive matter.

The combination of tannin with peptone is insoluble in the gastric juice, and this and the insoluble albumin tannates are decomposed in the alkaline juice of the intestine, the tannin forming alkaline tannates which possess little or no astringent action. If the free tannins reach the intestine after the administration of extracts of the crude drugs, they act on the mucous membrane, lessening intestinal secretion; this greatly modifies the bacterial development, and, therefore, the general intestinal conditions. Some of the metallic albuminates are soluble in an excess of proteid, and when in such a case the liberated acid is corrosive there is a penetrating corrosive action such as that of zinc or mercuric chlorid. With an insoluble precipitate, such as lead albuminate, which forms an impervious coating, and a mildly astringent acid, like acetic, there is a typical astringent and non-irritant effect.

The same astringent substance may be used in a

variety of conditions, and a number of different astringents are applicable to a given condition. A better acquaintance with the different tannins may lead to the selection of certain ones for particular cases, but at the present time we are guided more by the physical condition in which a given one is available; thus the official tannic acid is readily dissolved in the stomach, where it combines with the proteid of the content, or with the mucous membrane, whereas the tannin of gambir (gambir replaces the catechu of the Pharmacopeia of 1890) is protected by the presence of gum and extractives, and so passes into the intestine, there to exert its astringent effect. We can not attempt anything like a complete enumeration of the various uses of the astringents, but must content ourselves with summarizing briefly the principal indications of astringents and some of the chief characteristics of the more common remedies of this type.

USES OF ASTRINGENTS.

Astringents are used internally in the treatment of diarrhea and dysentery, in congestion of the mucous membrane of the stomach and intestines, and for hemorrhage in the alimentary canal and other directly accessible regions. The use of astringents —either organic or inorganic—for their effects on parts which can only be reached by way of the blood vessels is wholly irrational, and when benefit follows it is not due to the astringent action, since by their very nature astringents can not exist free in the blood in sufficient concentration to exert an astringent action. Traces of tannin are not astringent any more than they are irritant, and as-

tringents act only when brought into intimate contact with the tissue in sufficient concentration.

The metals are poisonous when absorbed, and, as a rule, vegetable astringents are to be preferred for internal administration, particularly when they must be used for a considerable period. Pure tannin, or tannic acid, as it is designated in the Pharmacopeia, may be used locally whenever a purely astringent action is indicated; for example, when secretion is excessive, and when it is desired to harden the skin in order to prevent excessive sweating.

The treatment of accessible, inflamed mucous membranes with antiseptic solutions, and more particularly with solutions of hydrogen dioxid, has greatly lessened the use of astringents, and the cleansing of an infected surface should be a routine procedure even when an astringent is to be applied subsequently. Dry tannin insufflated against an elongated palate often affords instantaneous relief.

Tannin in the pure state is rarely used internally because of its irritant action on the stomach, one of the preparations of astringent drugs being preferred in such cases. The dry powder acts as a styptic when applied to bleeding surfaces, but it must be borne in mind that tannic acid and all other astringents when given by mouth exert their astringent action only on the alimentary canal.

The various proprietary remedies, composed of tannin and albumin, gelatin or albuminoids, have not been shown to possess any decided therapeutic advantages over the official astringents, and several of the proprietary compounds, owing to their

variable composition, must necessarily be uncertain in their actions.

Tannic acid in simple solution combines with the albuminous contents of the stomach, and with the mucous membrane itself if the stomach be empty and the tannin in concentrated solution; it may then give rise to vomiting and even to diarrhea. This irritant action of the astringents leads to the use of several of them—alum, and zinc and copper sulphate—as emetics.

Tannin, being a precipitant of alkaloids, is useful as an antidote to those poisons when they are in the stomach—not when they have been given hypodermically, except possibly in the case of morphin, which is excreted into the stomach. The tannates thus formed are slowly broken up, and the stomach must be evacuated by emetics, or, preferably, by the stomach pump, as promptly as possible, tannin being added to the water which is used to wash the stomach after evacuation. Tea and coffee contain tannin, and, since they are almost universally available in emergencies, their use is very common. Torald Sollmann[1] determined the efficiency of infusions of tea and coffee as precipitants for various alkaloids and metals, and found the infusion of tea much the more active, but neither of them very reliable for the commonly used alkaloids, while the only metals for which tea (infusion) would be useful are mercury, lead and silver. As a single dose of lead never gives rise to acute symptoms, and as poisoning with silver salts is extremely rare, we must conclude that poisoning with mercuric salts is practi-

1. Journal of Medical Research, vol. vii, No. 1, p. 43.

cally the only instance likely to be encountered in which tea would prove to be an effective precipitant. The use of tea and coffee as stimulants in poisoning depends mainly on the caffein, and, of course, these remarks as to their limitations do not apply to the stimulant use of them.

VEGETABLE ASTRINGENTS.

ACIDUM TANNICUM.—U. S. P.—This is a light yellowish amorphous powder of a characteristic odor and a strongly astringent taste; it is very soluble in water, alcohol or glycerin.

Average dose: 0.5 gm. (8 grains).

GLYCERITUM ACIDI TANNICI.—U. S. P.—A 20 per cent. solution of tannic acid in glycerin.

Average dose: 2 c.c. (30 minims).

TROCHISCI ACIDI TANNICI.—U. S. P.—Each troche contains 0.06 gm. (1 grain) of tannic acid with sugar and tragacanth, flavored with orange-flower water.

GAMBIR.—U. S. P.—Gambir was introduced into the present Pharmacopeia to replace catechu of the earlier editions. It is an extract prepared from the leaves and twigs of *Ourouparia gambir* and occurs in irregular masses, varying in color from reddish brown to a pale brownish gray. It is inodorous, but has a slightly bitter, very astringent taste, with a sweetish after-taste.

Average dose: 1 gm. (15 grains).

TINCTURA GAMBIR COMPOSITA.—U. S. P.—This represents 5 per cent. of gambir and 2.5 per cent. of Saigon cinnamon in diluted alcohol.

Average dose: 4 c.c. (1 fluidram).

TROCHISCI GAMBIR.—U. S. P.—Each troche contains 0.06 gm. (1 grain) of gambir with sugar and tragacanth, flavored with orange-flower water.

KINO.—U. S. P.—The inspissated juice of *Pterocarpus marsupium* was introduced into medicine by Dr. John Fothergill about 1757.

Average dose: 0.5 gm. (8 grains).

TINCTURA KINO.—U. S. P.—The strength of this preparation has been reduced to 5 per cent. to obviate its tendency to gelatinize.

Average dose: 4 c.c. (1 fluidram).

The vegetable drugs that contain tannin are so numerous, and their general therapeutic actions are so similar, that we shall merely enumerate the following well-known vegetable astringents and official preparations:

RUBUS (blackberry-root bark).—Fluidextract and Syrup.

RED ROSE.—Fluidextract and Syrup.

GERANIUM.—Fluidextract.

HEMATOXYLON.—Extract.

RHUS GLABRA.—Fluidextract.

A combination of chalk which has attained very great popularity in the treatment of diarrhea is the

MISTURA CRETÆ.—U. S. P.—Chalk Mixture has the following composition:

Prepared chalk, 6 gm. (90 grains); powd. acacia, 4 gm. (60 grains); powd. sugar, 10 gm. (150 grains); cinnamon water, 40 c.c. (10 fluidrams), with water enough to make 100 c.c. (3 fluid-ounces).

The average dose is 4 teaspoonfuls (15 c.c.).

Chalk mixture is so well known that it is mentioned merely as a reminder of one of our best and simplest remedies for diarrhea. It is peculiarly adapted for combating the diarrhea of children. Severe cases may require the addition of a few drops of the deodorized tincture of opium to each adult dose or a suitable amount of paregoric (the camphorated tincture of opium) for children.

Troches of tannic acid are used almost exclusively in affections of the mouth and throat.

Gambir (catechu), kino, krameria and many other vegetable drugs contain large amounts of their peculiar tannins, together with mucilaginous and other extractive matter which tends to prevent the tannin from forming compounds in the stomach and thus preclude its action on the mucous membrane before it comes into the intestine, hence the preparations of these substances are more useful in the treatment of diarrhea than are pure tannin and its preparations.

Troches of gambir are well adapted for use in sore throat, after the throat has been sprayed with a solution of hydrogen dioxid, instead of the astringent gargles which were formerly so much in vogue.

Kino, like Gambir, may be given as a powder, preferably combined with opium and aromatics, as in the "Compound Kino Powder," N. F., which contains: Kino, 75; cinnamon, 20; powdered opium, 5 parts.

The following prescription, though somewhat complex, is a slightly modified form of one used in certain hospitals with satisfactory results; although the chalk is alkaline, it does not appreci-

ably lessen the astringency of the mixture, as do the carbonates of the alkalies which exist in the intestine. The compound tincture of gambir, or the tincture of krameria, may be used instead of the tincture of kino:

℞.	Cretæ præparatæ .....ʒi	4	
	Tincturæ kino .....ʒiv	15	
	Tincturæ opii.....m. v		3
	Spiritus chloroformi.....m. lxxv	5	
	Aquæ menthæ piperitæ.....ʒx	40	
	Syrupi aurantii q. s.....℥iii	100	

For children of from 3 to 10 years of age, from one-half to one teaspoonful of this mixture may be given every two or three hours; for adults the dose is one tablespoonful.

Gallic acid is sometimes recommended as an astringent, but it possesses no such action except that of any very weak acid, and it is absolutely useless for hemorrhage in the lungs, kidneys and other regions reached only by the circulation.

Though opium does not contain tannin, it would be a distinct omission if we failed to mention some of its indications in this place, since this work is intended primarily to call attention to the possible therapeutic uses of the official substances, and since the arrangement into groups, such as astringents, is merely for convenience. Small doses of any of the opium preparations afford one of the surest means of relief in diarrhea. They are commonly combined with astringents, inorganic, as well as organic, with excellent results, despite the chemical incompatibility existing between the alkaloids and the various tannins or metallic salts. The preparations of opium will be mentioned in the later chapters, and we now merely wish to call attention to methods of combining these agents.

℞. Tincturæ gambir compositæ.....ʒi 30 | 5
Tincturæ opii deodorati.....m. x
Bismuthi subnitratis .....ʒiiss 10
Aquæ camphoræ q. s.....℥iii 100

Sig.: One teaspoonful hourly for three or four hours, then every two or three hours.

Any one of the insoluble bismuth salts may be used, and tincture of kino or krameria substituted for the compound tincture of gambir. Similarly, an appropriate amount of the camphorated tincture of opium may be substituted for the deodorized tincture. When it is desired to give the same active ingredients in the form of a dry powder the following may be used:

℞. Opii pulveris.....gr. v | 3
Bismuthi subnitratis.....gr. cl 10
M. Et div. in chart. x.

Sig.: One powder to be given every two, three or four hours, according to the needs of the patient.

Here, again, the combination may be varied almost endlessly by using one of the other insoluble bismuth salts, the deodorized opium, or by adding a small proportion of one of the vegetable astringents like kino or gambir.

The pill of lead and opium is well adapted for securing a very slowly soluble form for administering these drugs. The pill is useful in diarrhea, but must not be long continued, lest it give rise to lead poisoning.

℞. Plumbi acetatis.....gr. xx 1 | 3
Opii pulveris.....gr. x | 6
M. Fac pilulas No. x.
Sig.: One pill to be given three or four times a day.

Inflammation of the stomach and intestine and gastric ulcer may be treated by an insoluble astringent powder which not only relieves congestion by its astringent property, but also forms an

insoluble protective covering, preventing the contact of irritating particles of food and the gastric and intestinal secretions, besides lessening the amount of these secretions.

METALLIC ASTRINGENTS.

The insoluble salts of bismuth are admirably adapted for the protection of the intestinal mucosa from irritants of various kinds. While as much as thirty times the average single dose of bismuth salts has been given in the course of a day, by the mouth, without any distinct evidence of untoward results, absorption and poisoning have followed the external use of bismuth salts as a dusting powder when used over a large surface.

Owing to the extremely poisonous nature of bismuth when absorbed, the soluble salts seem to us to be entirely superfluous, particularly as their solubility, until precipitation occurs, precludes the very object for which bismuth compounds are chiefly used—that is, for the mechanical coating of the surface with a protective layer of insoluble powder. It must be admitted, of course, that even the soluble salts of bismuth are astringent, but we have many safer astringents which are harmless that might well be used in their stead.

The activity of the nostrum-makers has resulted in placing on the market a number of preparations that are intended to combine the antiseptic properties of the benzene derivatives with the astringent properties of bismuth, but until we know more of the possibilities and the limitations of internal antiseptics it is preferable to use the simple astringents and to use our antiseptics separately.

BISMUTHI SUBNITRAS.[2]—U. S. P.—An insoluble white powder, without odor or taste.

BISMUTHI SUBCARBONAS.—U. S. P.—Closely resembles the subnitrate.

Average dose (of either salt): 0.5 gm. (8 grains).

BISMUTHI SUBSALICYLAS.—U. S. P.—This preparation closely resembles the subnitrate in physical properties and is intended to combine the antiseptic properties of the salicylic acid with the astringency of bismuth salts.

Average dose: 0.25 gm. (4 grains).

BISMUTHI SUBGALLAS.—U. S. P.—This preparation was at one time widely advertised and is even now occasionally prescribed by its proprietary name, dermatol. It occurs as a bright yellowish, insoluble, odorless and tasteless powder, which is mostly used externally as a substitute for iodoform.

It possesses the advantage over the subnitrate of

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2. A typical prescription for gastric irritation, or ulcer, is as follows:

℞.	Bismuthi subnitratis	grs. cl	10
	Mucilaginis acaciæ	ʒxii	50
	Aquæ cinnamomi q. s. ad	℥iii	100

M. Sig.: Shake well and take one or two teaspoonfuls three or four times a day.

In cases in which marked irritability persists, the addition of 0.01 gm. (1/6 grain) of cocain hydrochlorid to each dose, as a local anesthetic, may be advantageous, but we do not advise it as a routine procedure. For diarrhea one or two drops of the deodorized tincture of opium may be included for each dose, or, if preferred, tincture of opium. For this purpose, it is usually preferable to give one dose every hour for three or four doses, then every two to four hours as needed. Bismuth subcarbonate may be used instead of the subnitrate and tincture of kino, tincture of krameria or the compound tincture of gambir (catechu) may be added in the treatment of diarrhea.

not being very liable to absorption when used as a dusting powder.

Average dose: 0.25 gm. (4 grains).

PLUMBI ACETAS.—U. S. P.—Acetate of lead, or sugar of lead, is said to have been known to Geber. It was described by Raymund Lully in the thirteenth century, but was not used in medicine until introduced by Goulard a little more than a century ago. It occurs in crystals or as a heavy white powder, having an acetous odor and a sweetish, astringent, afterward metallic taste.

Average dose: 0.05 gm. (1 grain).

LIQUOR PLUMBI SUBACETATIS.—U. S. P.—An aqueous solution containing not less than 25 per cent. of lead subacetate.

LIQUOR PLUMBI SUBACETATIS DILUTUS.—U. S. P.—This contains about 1 per cent. of lead subacetate and is made by mixing 4 parts of the solution of lead subacetate with 96 parts of distilled water.

The official salts of zinc that are of interest as astringents are:

ZINCI SULPHAS.—U. S. P.—Colorless crystals, without odor, having an astringent metallic taste. Zinc sulphate is soluble in less than 1 part of water, but is insoluble in alcohol.

Average dose: Emetic, 1 gm. (15 grains).

ZINCI PHENOLSULPHONATE.—U. S. P.—The zinc sulphocarbolate of previous editions of the Pharmacopeia has been referred to under antiseptics.

Average dose: 0.12 gm. (2 grains).

ZINCI ACETAS.—U. S. P.—This is a widely used and deservedly popular astringent.

Average dose: 0.12 gm. (2 grains).

ZINCI OXIDUM.—U. S. P.—A white or yellowish-white powder, insoluble in either water or alcohol, it is largely used as a local application in dusting powders and in ointments, but is seldom given internally.

Average dose: 0.25 gm. (4 grains).

COPPER AND IRON SALTS.

CUPRI SULPHAS.—U. S. P.—Blue stone or blue vitriol was known to the Greeks as chalkanthos. Dioscorides described it as being a valuable astringent and, in large doses, emetic. It occurs as deep blue crystals that are devoid of odor, but have a nauseous, metallic taste. It is soluble in about 3 parts of water.

Average dose as an astringent: 0.01 gm. (10 mg. or 1/5 grain); as an emetic, 0.25 gm. (4 grains).

Of the numerous preparations of iron that have astringent properties we will mention but one, the chlorid, as representative of the whole class. This is official in several forms:

FERRI CHLORIDUM.—U. S. P.—This occurs in orange-yellow crystalline pieces, nearly odorless, but having a strongly styptic taste.

Average dose: 0.05 gm. (1 grain).

LIQUOR FERRI CHLORIDI.—U. S. P.—An aqueous solution of ferric chlorid, containing about 29 per cent. of the anhydrous salt.

Average dose: 0.1 c.c. (1½ minims).

This preparation is but little used, except for preparing

TINCTURA FERRI CHLORIDI.—U. S. P.—This is made by adding 35 parts of solution of ferric chlorid to enough alcohol to make 100 c.c. The official tincture is directed to be prepared at least three months before being used.

Average dose: 0.5 c.c. (8 minims).

This preparation is injurious to the teeth; therefore, it should be directed to be taken through a tube and the mouth rinsed with water or a very mild solution of an alkali, like lime water.

The only official preparation of silver that is of direct interest in connection with astringents is

ARGENTI NITRAS.—U. S. P.—This salt is supposed to have been known to Geber, but was introduced into medicine by Angelus Sala during the seventeenth century. It is very soluble in water and occurs as colorless, transparent, tabular crystals, that darken on exposure to light in the presence of organic matter. It is odorless, but has a bitter, caustic and strongly metallic taste.

Average dose: 0.01 gm. (10 mg., or 1/5 grain).

ALUMEN.—U. S. P.—Alum should contain not less than 99.5 per cent. of pure aluminum and potassium sulphate. It occurs as colorless crystals or as a white powder; it is odorless, but has a sweetish and strongly astringent taste. Alum is soluble in 9 parts of water, but is insoluble in alcohol.

Average dose: 0.5 gm. (8 grains).

ALUMEN EXSICCATUM.—U. S. P.—Popularly known as dried alum, must contain not less than 99 per cent. of anhydrous aluminum and potassium sulphate.

OFFICIAL LEAD SALTS.

Lead is of interest chiefly because of the chronic lead poisoning so often encountered.

The principal internal use of lead is in the form of the pill of the acetate, usually combined with opium, in the treatment of diarrhea. It has also been recommended for dysentery, but is not nearly so useful in that disease. This preparation should not be given for any considerable length of time, lest it give rise to chronic lead poisoning. The solution of lead subacetate is unfit for internal administration, but is of value in painful swellings and local inflammations and burns. The well-known mixture of laudanum and lead water has long been popular as an external application, but any mucilaginous liquid could probably be used in place of the tincture of opium without detriment, since the astringency of the lead is the main factor, the local application of the opium alkaloids being entirely superfluous because they are not absorbed from the unbroken skin. The local use of lead water itself is so thoroughly well established that it scarcely requires further comment.[3]

THE LOCAL TREATMENT OF MUCOUS MEMBRANES.

The local treatment of inflammation of the mucous membranes in the mouth, nose, throat, vagina and urethra, after thorough cleansing. preferably

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3. The following mixture will probably answer the purposes for which laudanum and lead water are commonly used:

℞. Liq. plumbi subacet.....min. lxxv 5
Mucil. acac. .....min. xiv 3
Aquæ q. s. ad.....f. ℥iii 100

The solution of lead subacetate is diluted with 55 c.c. (16 fluidrams) of water and the mucilage with 37 c.c. (10 fluidrams); the two are then mixed. Fifteen c.c. (4 fluidrams) of the water may be replaced by alcohol, but the amount of alcohol present in the mixture of laudanum and lead water is too small to be of any benefit.

with a solution of hydrogen dioxid, may require mild astringents of either organic or inorganic substances, though, as previously stated, the use of the solution of hydrogen dioxid has greatly lessened this necessity. Alum has long enjoyed a particular reputation in the treatment of stomatitis, and has also been used as a gargle, but it is injurious to the teeth, and the necessary solution, made of 1 part of alum in 20 parts of water, is preferably applied directly to the affected parts by means of a camel's-hair pencil or a swab made of absorbent cotton. After gargling, the mouth should be rinsed with water. Alum is not given internally so often as it was formerly; it is irritating and possesses no advantages over other astringents. Because of this irritant action it is emetic, and, while not very dependable, may serve in an emergency if no surer emetic is at hand. Small ulcerations of the throat, after having been cleansed with an antiseptic solution, may be touched with a mixture of 1 part of ferric subsulphate and 2 parts of glycerin, using a camel's-hair pencil or a cotton swab.

A very large number of astringent gargles are in common use, but the following is a good representative of the class:

℞.	Tincturæ ferri chloridi	m. cl	10
	Potassii chloratis	ʒiii	12
	Aquæ q. s	f℥vi	200

Those who object to the use of ferric chlorid may find the following preferable:

℞.	Glyceriti acidi tannici	f3v	20
	Aquæ q. s	f℥vi	200

Dried alum is used for the same purposes as alum, and, in addition, is somewhat caustic when dusted, as a dry powder, on exuberant growths.

THE USE OF ZINC SALTS.

Zinc sulphate and zinc phenolsulphonate may be considered together; they have a variety of applications, and it is only necessary to suggest the strength of the solutions that are to be used for various purposes.

For the eye they are generally used in the strength of from one-fourth to one-half of 1 per cent. in a solution of boric acid, to which camphor water may be added.

For the urethra strong solutions should not be used, one-half of 1 per cent. in water being sufficient. The popular combination of zinc sulphate and lead acetate, resulting in the insoluble lead sulphate and the very astringent zinc acetate, may possess some advantages over the more simple solution, but they are not very apparent.

Vaginal douches may be somewhat stronger and are frequently prescribed of from 1 to 2 per cent. strength.

As noted before, all the astringents may act as emetics if they are sufficiently irritant to the mucous membrane of the stomach and are not caustic. Zinc sulphate, however, deserves the preference among the astringents used as emetics. For this purpose it is usually given in doses of 1 or 2 gm. (15 to 30 grains) dissolved in a teacupful of warm water.

USE OF SILVER NITRATE.

Silver nitrate in the form of sticks, lunar caustic, is mainly used as a caustic for touching warts of various kinds and for non-granulating wounds. A solution of silver nitrate is sometimes used as an application to the conjunctiva, followed at once

by a solution of sodium chlorid, whereby a momentary action of the silver nitrate is obtained, the nitrate being instantly converted into the chlorid when the solution of sodium chlorid is applied.

Silver in combination with different proteids has been introduced under a variety of trademarked or proprietary names and recommended as a non-irritant antiseptic, mainly for the treatment of gonorrhea. Credé some years ago introduced a soluble form of metallic silver, for which certain manufacturers make the fabulous claim that it is an efficient disinfectant of blood and tissue. So long as septic diseases resist all treatment, it seems strange that reputable manufacturers will make such obvious misstatements.

The internal use of silver nitrate as an astringent is necessarily empirical, as the compound that is formed when silver nitrate is brought into contact with organic matter must be complex and problematic. A favorite pill of the late Dr. William Pepper for chronic gastritis was the following. It is submitted without comment:

℞. **Argenti nitratis**	
Extracti hyoscyami	
Mannæ, āā.....**gr. 1/3**	**02**

Fiat pilula No. i.

Such a pill was directed to be given three or four times a day, and the composition was occasionally varied by substituting powdered opium for the extract of hyoscyamus.

VASOCONSTRICTORS.

In addition to the astringent drugs depending on tannin or the metallic salts, certain alkaloids possess a markedly astringent, or, more properly,

vasoconstrictor, effect when applied to mucous membranes. Of these, the most useful are hydrastinin, a derivative of hydrastin, from which it is obtained by oxidation, and the alkaloid of the suprarenal gland. Here we are compelled to admit that this latter alkaloid, which is now being marketed at the modest price of some $800 per ounce, despite Abel's simple and inexpensive method of preparation, is superior to the official desiccated suprarenal gland. The application of a 1 to 1,000 solution of hydrastinin or a 1 to 5,000 solution of the suprarenal alkaloid, in 0.9 per cent. solution of sodium chlorid, to an inflamed conjunctiva or inflamed nasal mucous membrane often affords prompt relief. In view of the very great difference in cost without a corresponding difference in effect, the physician can well afford to use hydrastinin in preference to the more expensive alkaloid in such conditions.

The desiccated suprarenal gland may be macerated in water and the fluid filtered and used, but any of the preparations of the alkaloid which appear under a variety of trade names will usually be preferred. Slight hemorrhages are also stopped by either of these means.

When the flow of blood is copious and hot water is ineffective, styptics are useful; they are not alone astringent, but also cause a sudden coagulation of the blood, and this plugs up the orifice. Large clots must be removed, as they prevent the immediate contact of the astringent or styptic and may conceal a hemorrhage occurring in cavities—the uterus, for instance—in which case the clot may fill the upper part of the vagina.

It is necessary to bear in mind the difference between the action of vasoconstrictors, like the alkaloid of the suprarenal gland, and the action of styptics, like tannin or the ferric salts. With the former the action is transitory and the hemorrhage may recur as soon as the action of the drug has worn away, while styptics, when effective, form a plug in the normal distended blood vessel. Another point to be remembered, in this connection, is the fact that the absorption of a vasoconstrictor, following its continued or too liberal use, will cause a general rise of blood pressure and thus actually increase the flow of blood at the bleeding points.

At least one death following an injection of adrenalin has been attributed to that drug. The patient died eight days after adrenalin and cocain had been used in the extraction of a carious tooth.

GLANDULÆ SUPRARENALES SICCÆ.—U. S. P.—Desiccated Suprarenal Glands are directed to be obtained from the sheep or ox, freed from fat, cleaned, dried and powdered. One part of desiccated suprarenal gland represents approximately 6 parts of fresh glands free from fat.

Average dose: 0.25 gm. (4 grains).

The alkaloid contained in the suprarenal glands has been variously designated as epinephrin by Abel, suprarenin by Fürth and adrenalin by Takamine. The trade names that are now applied to the solutions of the same substance are legion, and it seems very unfortunate indeed that the committee on revision of the Pharmacopeia did not recognize the alkaloidal substance in an official way and give it an official title. The only effect to be ex-

pected from the internal administration of the gland or its alkaloid is the local constriction that is noticed when it is applied to the mucous membrane. The solution of the alkaloid is without effect on blood pressure when given by the stomach and when injected just beneath the skin it produces practically no effect, except a local vasoconstriction. The dried gland is unsuited, of course, for intravenous use.

CHAPTER IX.

IRRITANTS, EMOLLIENTS AND DEMULCENTS.

There are so many substances which have been used as irritants under varying conditions that we can not attempt to do more than mention the more useful of the agents frequently employed for this purpose, together with some of the conditions in which clinical experience has shown them to be most beneficial.

While the employment of counter-irritants is almost wholly empirical, the regions of the skin which Brunton has indicated for their use when it is desired to influence the internal organs correspond well with those which Head has shown to exhibit tenderness of the skin in connection with diseases of the same organs.

Brunton directs the irritant to be placed over the larynx, ovaries or sciatic nerve for affections of those parts, over the ensiform cartilage for gastric disturbance, above and below the knee in rheumatism, over the ball of the great toe (dorsal surface) in gout, behind the ear in facial neuralgia, at the base of the brain and back of the neck for cerebral affections, and along the dorsal region to affect the uterus.

The mildest of irritants is water or saline solution used as a bath. The shock of the cold water applied to the skin and the slight irritation of the subsequent friction, preferably with a coarse towel,

are followed by a reaction attended with a considerable and lasting stimulation. Very cold water may produce too great a shock in persons who are not robust, and the result will be depression, but there can be little doubt that baths are extremely beneficial when the temperature is so regulated that a healthy glow and a feeling of well-being succeed. It seems that the question of the usefulness or the harm of cold baths, about which there has been so much contention, resolves itself into a question of individual experience. If a feeling of exhilaration, but no subsequent depression, follows the bath it is not harmful; if no such exhilaration occurs, but a distinct depression is observed, there can be but little doubt that the bath is doing harm. In such cases a slight increase in the temperature of the water, with a shorter time and more rubbing, may secure the benefits sought. The same person may require different conditions of temperature at different times, corresponding to variations in the general health.

A mixture of salts is sometimes added to the bath to increase the slight irritant action.

Even milder than the friction, which forms so essential a part of the bath, is the irritant action of the astringents, which have been discussed in Chapter VIII, but these are followed by lessened irritation, hence they are not considered among the irritants.

RUBEFACIENTS.

Rubefaction is the result of a slight irritation of the skin. There is a slight increase in the exudate from the capillaries, and if the irritation be not

long continued this exudate is reabsorbed and the part speedily returns to the normal condition.

While all irritants, mild and caustic, cause rubefaction, we shall first consider those which are used for that stage alone, and take up the vesicants, pustulants and caustics later.

ALCOHOL.

Alcohol alone, diluted with water or in the form of hamamelis water, alcoholic tinctures, spirits or liniments, is used more frequently, perhaps, than any other mild irritant, with the possible exception of the bath.

Applications containing alcohol are useful in painful swellings, bruises and a great variety of minor complaints commonly treated in the household without calling on the physician.

While it is probably quite unnecessary, at this late date, to call particular attention to the fact that there is a very great difference between the official, or ethyl, alcohol and the various forms of wood, or methyl, alcohol, nevertheless the insidiously poisonous properties of the latter substance do not appear to be well appreciated by the general public. The number of cases of blindness and of death that have been reported by Buller and Wood[1] amply demonstrate that even the external use of any form of wood alcohol is not entirely free from danger and that its use in any form of medicinal preparation should not be countenanced or tolerated.

Among the numerous preparations of the

1. THE JOURNAL A. M. A., Oct. 1, 8, 15, 22 and 29, 1904.

United States Pharmacopeia that have been used as topical applications, largely because of the rubefacient properties of the alcohol that they contain, we may enumerate:

AQUA HAMAMELIDIS.—U. S. P.—This preparation, more popularly known as extract of witchhazel, or distilled extract of witchhazel, is now, for the first time, included in the Pharmacopeia. While the preparation itself has been known for many years, and has been used extensively as a household remedy, it has never met with much favor on the part of the medical profession. The official preparation is directed to contain 15 per cent. of alcohol and should be free from methyl alcohol or any of its derivatives.

TINCTURA ARNICÆ.—U. S. P.—Tincture of arnica represents 20 parts of the dried and powdered flower heads of *Arnica montana* in diluted alcohol. This preparation was at one time very popular with medical practitioners as a topical application in so-called "sprains" and in bruises, but is now seldom employed. The same is true of:

TINCTURA CALENDULÆ.—U. S. P.—This preparation represents 20 per cent. of the dried and powdered florets of *Calendula officinalis,* the well-known marigold of our gardens.

Probably the most objectionable feature in connection with the use of any of the official tinctures as topical applications is their tendency to stain. This objection is largely overcome by the use of the simple diluted alcohol, one of the numerous unofficial toilet waters or colognes, or by the use of one or the other of the official spirits.

In addition to

SPIRITUS FRUMENTI.—U. S. P.—Whisky, and

SPIRITUS VINI GALLICI.—U. S. P.—Brandy, the most frequently used of this class of preparations is:

SPIRITUS CAMPHORÆ.—U. S. P.—This is an alcoholic solution containing 10 per cent. of camphor.

SPIRITUS GAULTHERIÆ.—U. S. P.—This contains 5 per cent. of oil of gaultheria in alcohol.

The most widely used, as well as the most popular, of the mildly rubefacient liniments of the Pharmacopeia is:

LINIMENTUM SAPONIS.—U. S. P.—Soap Liniment is variously known as liquid opodeldoc, camphorated soap liniment and camphorated tincture of soap. It contains 6 parts of soap, 4.5 parts of camphor, 1 part of oil of rosemary and 72 parts of alcohol with sufficient water to make 100 parts. This preparation has long been popular as a topical application and is not infrequently used as a vehicle for other more active rubefacients, sedatives and anodynes.

A somewhat typical compound liniment is the

LINIMENTUM CHLOROFORMI.—U. S. P.—This is a simple mixture of 30 parts of chloroform with 70 parts of soap liniment, and constitutes a very good illustration of the possible uses of soap liniment as a solvent or vehicle.

CHLOROFORM.

Chloroform is one of the more active rubefacients and the action quickly passes this stage if its use be continued. Chloroform readily dissolves fat, and, being very volatile, it penetrates quickly,

causing considerable redness and pain. A few drops of chloroform placed on a little absorbent cotton and applied over a painful joint, such as a bunion, in such a way that evaporation of the chloroform is prevented, causes a good deal of pain but often affords speedy relief. It should not be applied in this way for longer than ten or fifteen minutes. Chloroform may be used as a counter-irritant by putting a few drops on cotton in a wide-mouthed bottle and applying the mouth of the bottle to the area to be treated for a few minutes at a time.

Chloroform liniment, noted above, is much less painful, or not at all so in most cases, and is much slower in producing its effects. Chloroform liniment is usually directed to be applied to the affected part by being thoroughly rubbed in, thus securing the additional rubefacient action of friction. It may, however, be more economically applied, and is frequently quite as effective, if directed to be put on cotton, applied to the affected surface and then covered with several layers of cloth or otherwise prevented from evaporating too rapidly.

VOLATILE OILS.

All the volatile oils are irritant, their action ranging from that of the mild sandalwood or copaiba oil to the extremely irritant volatile oil of mustard or even the caustic action of oil of cloves. The use of the milder members of this series for their effects on the urinary tract will be mentioned in connection with diuretics. Some of the volatile oils, such as pennyroyal and savin oils, which are somewhat more irritant, have been employed to

produce abortion by reason of irritation of the intestine and the consequent participation in the effects by the uterus.

Of the official substances that are more or less closely connected with the turpentine group and are frequently used externally, we have:

OLEUM ROSMARINI.—U. S. P.—This is a volatile oil distilled from the fresh flowering tops of *Rosmarinus officinalis* and is one of the ingredients in the well-known soap liniment.

OLEUM SABINÆ.—U. S. P.—Oil of Savin has been quite extensively used as a local irritant. It must be used with caution in order to guard against the tendency to act as a vesicant.

OLEUM TEREBINTHINÆ.—U. S. P.—Oil of Turpentine is the volatile oil distilled from turpentine. Even as an external application it is not infrequently used in the form of

OLEUM TEREBINTHINÆ RECTIFICATUM.—U. S. P.—This is identical with oil of turpentine in chemical properties, but it has a more agreeable odor.

TEREBINTHINA.—U. S. P.—This is officially described as the concrete oleoresin of *Pinus palustris* and of other species of *Pinus*.

RESINA.—U. S. P.—Rosin, resin or colophony, is the residue left after distilling off the volatile oil from turpentine. The last two articles, rosin and turpentine, are interesting only as constituents of several official preparations, of which the best known are:

CERATUM RESINÆ.—U. S. P.—This is a cerate containing 35 parts of rosin, 15 parts of yellow wax and 50 parts of lard.

CERATUM RESINÆ COMPOSITUM.—U. S. P.—This is a revival of the one-time official Deshler's salve. It contains rosin, yellow wax, prepared suet, turpentine and linseed oil.

LINIMENTUM TEBEBINTHINÆ.—U. S. P.—This is a solution of 65 parts of resin cerate in 35 parts of oil of turpentine. It has been recommended to be used in place of the oil of turpentine as a local application when the action of the latter might be considered as too irritating.

Plasters of Burgundy pitch, Burgundy pitch with cantharides and of resin were formerly official. In practice these old-time resin plasters have long since been replaced by the more modern rubber-base plasters.

CAPSICUM.

CAPSICUM.—U. S. P.—The dried ripe fruit of *Capsicum fastigiatum* constitutes one of the most popular of the rubefacients used at the present time. Of the available official preparations we have:

FLUIDEXTRACTUM CAPSICI.—U. S. P.—This is made with strong alcohol.

TINCTURA CAPSICI.—U. S. P.—This is made with a mixture of 95 parts of alcohol with 5 parts of water, and represents 10 per cent. of the crude drug.

Either of these preparations may be used diluted with alcohol or with soap liniment as a local rubefacient or irritant.

OLEORESINA CAPSICI.—U. S. P.—This is made by extracting capsicum with acetone and may be used in the shape of the plaster, as noted above, or

in the form of the now popular mixture with petrolatum.

The best representative of the rubefacient plasters now in use is the

EMPLASTRUM CAPSICI.—U. S. P.—This is directed to be made by applying a thin coating of oleoresin of capsicum to adhesive plaster.

MENTHOL.

MENTHOL.—U. S. P.—This is a secondary alcohol obtained from the oil of *Mentha piperita* or other mint oils.

CAMPHORATED CHLORAL.—N. F.—This preparation, quite popular in some parts of the United States as a local application, consists of equal parts of hydrated chloral and camphor. It is a thick, oily-looking liquid, which is extremely irritating. It may be diluted with the fatty oils, alcohol or soap liniment.

MUSTARD.

Mustard is official as:

SINAPIS ALBA.—U. S. P.—White Mustard is the seed of *Sinapis alba.*

SINAPIS NIGRA.—U. S. P.—Black Mustard is the seed of *Brassica nigra.*

OLEUM SINAPIS VOLATILE.—U. S. P.—This is a volatile oil obtained from black mustard (freed from its fatty oil) by maceration with water and subsequent distillation.

CHARTA SINAPIS.—U. S. P.—Mustard Paper is directed to be made by coating rather thick, well-sized paper with a mixture of rubber cement and powdered black mustard which has been deprived of its fatty oil.

Mustard foot baths, containing one or two ounces of powdered or ground mustard, preferably the black, thoroughly mixed with a gallon of warm water, are extremely useful for the relief of mild congestions of the head and of the gastro-intestinal tract.

Prompt relief is often obtained in this way from headache and from pain in the stomach. In many cases, even mild attacks of indigestion show decided improvement almost immediately; the action is further accelerated if a hot-water bag is placed over the region of the stomach at the same time.

The feet should be placed in the bath while the legs and feet are briskly rubbed with the mustard water for ten minutes or until the skin is red and some irritation is felt. The extremities are then rubbed dry with a coarse towel and wrapped in flannel or a blanket. When a slight degree of counter-irritation is desired for some time, a mustard poultice is employed. This is made by mixing one part of the ground black mustard with about five parts of flour (or ten parts of flour in the case of children), and mixing with enough water to form a mass. This is then spread on cheesecloth and applied at once.

Mustard poultices have been largely replaced by the much more convenient mustard papers, which are dipped in tepid water and applied at once. They are prone to become worthless in damp climates, since the absorption of moisture causes the slow development of the volatile oil, which then evaporates as fast as it is formed. With proper precaution, however, they may be preserved for a

considerable length of time, and they will usually be found to afford the most convenient means of applying counter-irritation.

Baths are used for their tonic and antipyretic action. The importance of friction—rubbing with a towel—after a bath can not be insisted upon too strongly, for the cold bath is potent for much harm in certain conditions, and the patient may pass into collapse if the proper technic is not observed in such cases. The antipyretic effect is only one, and perhaps even a minor, use of the bath in typhoid fever. The tonic effect is absent, and much injury may be done when the cutaneous circulation, as evidenced by the redness of the skin, is not re-established after the bath.

The regular use of the cold bath in the morning is very commonly supposed to lessen the tendency to catch cold.

Mild rubefacients, such as alcohol, soap liniment, tincture of arnica and hamamelis water, are used for bruises and painful swellings. They induce redness of the skin and temporary changes in the cutaneous circulation, but their use beyond this stage is not indicated in these affections.

Oil of turpentine may be applied either in the form of the official liniment, diluted with a fatty oil, or it may be used in substances as a stupe; the latter is made by saturating a cloth with hot water, wringing it out and then dropping on it a little oil of turpentine, or dipping the moist cloth into the oil of turpentine and again wringing it out and applying while still warm.

Local applications of this kind will be found useful in bronchitis.

Oil of turpentine is used internally, and it is applied as a stupe externally for the excessive flatulence often seen in typhoid fever; the liniment of turpentine is occasionally used as a protective in the treatment of burns.

Resin cerate and the compound resin cerate are used to stimulate indolent ulcers such as are often seen after burns and scalds.

Spirit of camphor may be used in much the same way, as well as by local application for headache and neuralgia.

Chloroform, particularly in the form of the liniment, is useful as an anodyne in painful inflammations of the superficial tissues, but its evaporation must be prevented by an impermeable covering, such as oiled silk.

Capsicum plaster and other rubefaçients are used for muscular rheumatism, neuralgia and colic.

Menthol in cones, or in alcoholic or ethereal solution, is applied to the skin for headache and neuralgia. It causes a burning sensation and then that of coolness.

Oleoresin of capsicum may be used as a rubefacient in the form of an ointment made as follows:

℞.	Oleoresinæ capsici	gr. xv	1
	Petrolati	℥iii	100

M. Ft. unguentum.
Sig.: Use locally.

Chloral camphor is an active rubefacient, but it is said never to cause blistering. It is used in toothache and in neuralgia.

HEAT.

The uses of heat are so numerous and so well known that they scarcely require further mention at this time. We may be permitted to call attention, however, to some of the various forms of cataplasms or poultices that are frequently used for their rubefacient or irritant properties.

Among the official substances that are frequently used for the preparation of poultices we have:

LINUM.—U. S. P.—Linseed or flaxseed is the ripe seed of *Linum usitatissimum.*

ULMUS.—U. S. P.—Elm or slippery elm is the dried bark of *Ulmus fulva,* deprived of its periderm.

CARBO LIGNI.—U. S. P.—This is charcoal prepared from soft wood and powdered.

Poultices are ordinarily prepared by mixing the requisite amount of ground flaxseed, ground elm bark or other substance with enough boiling water to make a rather stiff mass, inclosing this in a piece of gauze or muslin and applying to the surface as hot as it can be borne.

The rubefacient properties of a poultice may be increased by the addition of ground mustard, tincture of capsicum or of oil of turpentine. For removing fetor or to act as disinfectants, poultices may have added to them powdered charcoal, chlorinated lime or the official solution of chlorinated soda.

The present edition of the United States Pharmacopeia has included one poultice, as:

CATAPLASMA KAOLINI.—U. S. P.—This consists of kaolin, glycerin and boric acid, with thymol, methyl salicylate and oil of peppermint as

admixture to give it a pleasing odor. This preparation, like other poultices, is most efficacious when applied hot, but, as its action depends to a very great extent on the rubefacient properties of undiluted glycerin, due precaution should be taken to prevent the absorption of water or of watery vapor during the course of preparation or when heating it preparatory to applying.

Practically the same preparation is being offered to the medical profession at the present time under a variety of trade names, and, while the combination undoubtedly has uses, many, if not all, of the positive claims that are made in connection with it are, to say the least, somewhat exaggerated, and the preparation should not be expected to accomplish more than might reasonably be expected from an equivalent application of heat and mild rubefacients.

One other point in connection with this particular preparation that has been the cause of some controversy in the advertising pages of medical journals is the question of priority. This question may safely be ignored, as the mixture, apart from the flavoring ingredients, can not be said to be new. Glycerin magmas have been known and used for upward of half a century, and a formula for practically an identical preparation may be found in the *Pharmaceutical Journal,* London, for March, 1858.

Formic acid has long been known and used in domestic practice as a rubefacient. In Germany it has found considerable favor in regular medicine and is official in the German Pharmacopeia as a 24 per cent. solution and also as a spirit of formic

acid, the latter containing 4 per cent. of the official solution of formic acid in a mixture of alcohol and water.

IODIN.

The official preparations of iodin that are used as rubefacients are:

LIQUOR IODI COMPOSITUS.—U. S. P.—This is better known as Lugol's solution; it contains 5 per cent. of iodin and 10 per cent. of potassium iodid in water.

TINCTURA IODI.—U. S. P.—This is an alcoholic solution and contains 7 per cent. of iodin and 5 per cent. of potassium iodid.

UNGUENTUM IODI.—U. S. P.—This contains 4 per cent. of iodin and 4 per cent. of potassium iodid in a mixture of glycerin and benzoinated lard.

Iodin in the form of the tincture or of the solution is very commonly applied to the skin as a counter-irritant. Repeated applications produce a caustic effect, but the action is very easily controlled. One great disadvantage possessed by the official preparations of iodin is the dark staining of the skin. Numerous efforts have been made to obviate this by using so-called colorless tinctures of iodin, which are merely solutions of iodids. It is much better to apply the iodin until sufficient irritation is caused and then remove the stain by washing with dilute solution of ammonia water or with a solution of sodium thiosulphate.

A more modern preparation of iodin that promises to replace the official preparations as an external application is a solution of iodin in saponated petrolatum, a formula for which will be

found in the latest edition of the National Formulary.

Saponated petrolatum may be made by simply mixing:

Liquid petrolatum	℥ii	60
Oleic acid	℥i	30
Spirit of ammonia	℥ss	15

in the order enumerated, the only necessary precaution being to use preparations that correspond to the requirements of the United States Pharmacopeia.

This simple saponated petrolatum will readily dissolve iodin up to 10 per cent. of its weight. A 5 or 6 per cent. solution of iodin, however, will be found to be the most useful and not too irritating.

Probably the greatest advantage possessed by a preparation of this kind is due to the fact that it causes little or no stain and may be readily washed off with soap and warm water.

Saponated petrolatum may also be used for applying a number of other rubefacients, such as camphor, menthol, chloroform, methyl salicylate and turpentine.

The ordinary hot water bag has come into such general use for the application of heat that its mention is almost superfluous, but we will be permitted to remind the practitioner of the fact that this affords one of the most cleanly means of securing rubefaction. Wakefulness due to cold feet may be prevented by the use of a hot water bag. Those covered with flannel or the plain bag wrapped in cloth retain the heat much longer and are much less liable to produce burns.

The temperature of the hot water bags should

be regulated with care, as burns are not uncommon. The bag should not be used when it is too hot to be borne against the cheek.

VESICANTS.

Vesication is the result of greater irritation than that which merely causes rubefaction. The exudate from the blood vessels is not absorbed, but collects beneath the horny layer of the skin, which it can not penetrate, but which it separates from the layers beneath. Such collections of fluid are called vesicles or blisters, and the agents which produce them are termed epispastics, vesicants or "blisters."

If the vesicle is ruptured soon after it has formed, and the horny layer removed, it leaves a tender surface of the skin exposed; this is irritated even by contact with the air, and, being easily permeated, it is liable to infection, hence it is better to puncture the blister with a sterile needle inserted at the periphery; the fluid is allowed to escape while the loose layer of epidermis is left in place for protection until a new hard layer is formed.

While there is some sensory stimulation, vesication may occur, with merely an itching, from slowly acting agents which do not penetrate readily.

Those agents which, applied to the skin, cause vesication also cause an irritation of the mucous membrane, but, as the exudate escapes more readily from such surfaces vesication does not usually occur.

Vesicants, and, in fact, all but the mildest of

irritants, such as heat, are contraindicted in the treatment of infants, in diabetics, who are prone to gangrene, and for the old and feeble.

The internal use of irritants which are excreted by the kidneys, and their external use if they are absorbed, as sometimes occurs with cantharides, are to be avoided in nephritis; in such cases stronger ammonia water may be used, but it is very painful.

Mustard occasions so much pain before blistering, owing to the volatility of the oil of mustard, which, therefore, penetrates readily, that it is seldom used to produce an irritation beyond the stage of rubefaction.

Cantharides contains cantharidin, which, though readily volatile at a higher temperature, is not much affected at the body temperature and does not rapidly penetrate the tissues, hence cantharides causes vesication with but little pain and is much the most popular of the vesicating agents.

OFFICIAL PREPARATIONS OF CANTHARIDES.

CANTHARIS.—U. S. P.—Cantharides, more popularly known as Spanish flies, is officially described as the thoroughly dried beetle of *Cantharis vesicatoria.* The powder of cantharides, which is the form of the drug that is most frequently found in the shops, is grayish brown in color with shining green particles. It should contain few or no hairs.

CERATUM CANTHARIDIS.—U. S. P.—Cantharides Cerate, also known as blistering cerate or blistering plaster, contains 32 parts of powdered

cantharides in a mixture of liquid petrolatum, yellow wax, rosin and lard. Cantharides cerate is most frequently used in the form of a plaster, spread on the official adhesive plaster or some other suitable grease-proof material.

COLLODIUM CANTHARIDATUM.—U. S. P.—Cantharidal Collodion represents the chloroform soluble portion of 60 parts of cantharides dissolved in sufficient flexible collodion to make 100 parts.

TINCTURA CANTHARIDIS.—U. S. P.—This preparation represents 10 parts of cantharides extracted with alcohol. It is not usually efficient as a vesicant, but is frequently used externally as an irritant or rubefacient.

The active principle of cantharides is not soluble in water, and, as the normal skin is usually covered with a thin film of perspiration, the necessary precautions must be taken to have the blistering preparation come in contact with the dry skin.

This is most readily accomplished by washing the part with soap and water and wiping it with a small amount of strong alcohol. In the case of the cerate or plaster the alcohol may be followed by a fatty oil, or, better still, the surface of the plaster may be thinly coated with a coating of oil.

In directing the use of a blister it should be remembered that the resulting vesicle is usually larger than the plaster that has been applied, and the size of the latter, therefore, should be gauged accordingly.

Cantharidal collodion is simply painted on the surface, and is more cleanly than the cerate. In using blistering collodion the same precaution of

thoroughly cleansing the skin, with soap and water, and alcohol, should be observed so as to insure vesication.

Vesication usually ensues in about six hours after the application of the vesicant, but a somewhat longer period may elapse even in cases in which all the necessary precautions have been observed, and the physician should allow ample time before he concludes that the preparation is worthless.

Cantharides is prone to deteriorate with age, and one is often inclined to attribute the failure to cause blistering, to the worthlessness of the product, but even a faultless preparation may at times fail to produce vesication.

The now widely used rubber-base plaster containing cantharides, although not official, has many points of advantage over the less cleanly extemporaneous plaster made from the cerate. After preparing the surface of the skin, as indicated above, the plaster is smeared over with a thin film of oil and applied at once. After causing sufficient vesication it can be removed readily, and in this respect offers some advantage over the blistering collodion which continues to act until exhausted.

While cantharides is commonly employed as a vesicant, it is sometimes applied for a shorter time to produce rubefaction, and its irritant action is also made use of in hair tonics, as it is supposed to stimulate the growth of hair.

The following formula fairly represents the form of mixture commonly used as a hair tonic:

℞.	Tincturæ cantharidis	f℥ii	8
	Ammonii carbonatis	ʒi	4
	Spiritus myrciæ	f℥ii	60
	Aquæ q. s. ad	f℥vi	200

M. Sig.: Apply with brush, rubbing into the scalp after washing with tar soap.

For this preliminary cleaning, or shampooing, the expensive Packer's tar soap has no advantage over the very much cheaper tar soap generally used by machinists for washing grease from the hands.

Cantharides is commonly recommended for the treatment of baldness, but, like every other agent used for this purpose, it is usually ineffective.

Where an oleaginous preparation, containing cantharides, is desired, the following may be used:

℞.	Olei ricini		
	Tincturæ cantharidis, āā	f℥ii	8
	Spiritus myrciæ	f℥i	30
	Alcoholis q. s. ad	f℥vi	200

M. Sig.: Apply locally to scalp.

The toxicology of cantharides is of some importance because the laity has an exaggerated idea of its efficiency as an aphrodisiac without a corresponding appreciation of its harmful effects on the kidneys.

Poison oak has been used as an irritant, but it is wholly unsuited for the purpose because of the extraordinary activity of the irritant principle, the uncertainty of its action, and the inability to control it, which render it far inferior to many other available irritants.

It is of considerable toxicologic interest because of the frequency with which accidental poisoning occurs, either from handling it or merely coming into the immediate neighborhood, since even dust

[illegible] of the [illegible] or glucoside which [illegible] and [illegible] is the active substance [illegible] the action depends to poison susceptible persons.

[illegible] penetrates the skin very easily [illegible] difficult to remove. Even bland [illegible] in the treatment of poisoning [illegible] to dissolve and spread [illegible] of course, of [illegible].

[illegible] poisoning as much as [illegible] should be removed by repeated washing with soap and fresh portions of warm water after which a paste of soap or a solution of lead acetate is applied. If vesicles form [illegible] be opened with care and the liquid [illegible] or a powder such as [illegible] would but extend the irritation [illegible] liquid were allowed to spread [illegible] surface of the skin.

[illegible] a solution of potassium permanganate in numerous cases of intentional and accidental poisoning on himself, and found it uniformly effective. He rubbed a 1 per cent. solution of the permanganate into the vesicles, whereby the poison was destroyed by oxidation. He found it very much more effective when the part affected was immersed for a time in a hot solution of the permanganate. The resulting staining of the skin is a small matter compared to the discomfort of the poison in severe cases, but this stain may be removed with a solution of oxalic acid.

The place should then be carefully washed with

soap and warm water to remove even traces of the fluid from the vesicles, and the soap paste or the solution of lead acetate applied.

Fluidextract of grindelia robusta, diluted with water, or with a saturated solution of sodium bicarbonate (about 6 per cent.) has had a special reputation as a wash for the treatment of poison oak.

PUSTULANTS.

Pustulants are those irritants which give rise to pustules instead of vesicles. The pustulants appear to be unable to affect the skin through the horny layer as a rule, but can only penetrate the orifices of the glands. They are much less frequently used than the rubefacients and the vesicants.

As tartar emetic is not irritant except in acid solution it has been suggested that it is decomposed by acids in the cutaneous glands, and there produces pustulation.

Croton oil owes its irritant action to crotonoleic acid, which exists mainly in combination as a fat. This fat is not affected by the gastric juice, but is split up in the intestines and the crotonoleic acid is then able to exert its violent irritation resulting in purgation.

Applied to the skin croton oil causes pustulation. It is not now so much used externally or internally as it was formerly.

OFFICIAL PUSTULANTS.

ANTIMONII ET POTASSII TARTRAS.—U. S. P.—Antimony and Potassium Tartrate, more commonly known as tartar emetic, is usually seen as a

white granular powder, without odor, and having a sweet, afterward disagreeable metallic taste. It is soluble in about 16 parts of cold water, but is much more readily soluble in hot water.

Antimony and potassium tartrate may be used externally, as a pustulant, either in the form of the powder, in aqueous solution, or in the form of an ointment. The German Pharmacopeia contains a formula for the latter preparation that appears to be quite popular on the continent of Europe. This is a simple mixture of 20 parts of antimony and potassium tartrate, with 80 parts of petrolatum.

Because of its irritant action tartar emetic produces nausea or emesis, when taken internally, ac-according to the amount employed. It is much more frequently used as a nauseant than as an emetic, and least often as a pustulant; for the latter purpose it will be found to be preferable to use it in the form of an ointment, similar to the one referred to above, simply rubbed on the skin.

OLEUM TIGLII.—U. S. P.—Croton oil is described as a fixed oil expressed from *Croton Tiglium.* It occurs as a pale yellow, or brownish yellow, viscid, fluorescent liquid, having a mild, oily, afterward acrid and burning taste. In eastern countries croton oil appears to have been known from a very early period. It was known in Europe several centuries ago, but fell into disuse and was reintroduced there with several other drugs from India, about 1813.

CAUSTICS.

Caustics are irritants which either cause violent inflammation, resulting in necrosis, or dissolve the tissue by direct chemic action.

Caustics may be used to produce counter-irritation alone, to remove exuberant or diseased tissue, or, in diluted form, to stimulate non-granulating surfaces.

Apart from the use of the thermocautery in surgery, that of lunar caustic for exuberant growths and non-granulating tissues, and of arsenic for the destruction of the nerves of teeth, caustics are not very widely used at the present time.

The number of substances possessing a corrosive action is, of course, very great, but many of them are not suited for therapeutic use, thus the strong alkalies, such as caustic potash and caustic soda, dissolve the tissue and penetrate deeply, hence their action is not easily controlled, besides they are very painful.

Potassium hydroxid, better known, perhaps, as potassa, is sometimes used to soften and to remove the callus of corns and warts.

The action of silver nitrate, and of copper sulphate, in the form of molded sticks, or cones, is so easily controlled that they are very commonly used.

ARGENTI NITRAS.—U. S. P.—Silver Nitrate, which appears to have been known to Geber as lapis infernalis in the eighth century, has been used extensively. It occurs as colorless crystals, which are freely soluble in about one part of water and melt or fuse at 200° C. (392° F.). This latter feature is taken advantage of in making the official forms of fused silver nitrate, and is also of advantage in forming extemporaneous preparations, for local application, by melting or fusing

silver nitrate on to suitable metallic instruments such as sounds.

ARGENTI NITRAS FUSUS.—U. S. P.—Molded Silver Nitrate contains about 95 per cent. of silver nitrate, with a small amount of silver chlorid, which is added to make the sticks tough and fibrous.

ARGENTI NITRAS MITIGATUS.—U. S. P.—Mitigated Silver Nitrate is composed of one part of silver nitrate and two parts of potassium nitrate fused together.

CUPRI SULPHAS.—U. S. P.—Copper Sulphate or blue vitriol occurs as large, transparent deep blue crystals. For external use these crystals may be rasped or filed into suitable shape, and are then used in very much the same way as are the sticks of silver nitrate.

The various uses of these agents are so well known that they scarcely require extended treatment here.

When the lunar caustic is used on exuberant granulations care should be taken to avoid bringing it into contact with the newly formed skin, which is recognized only as a bluish line, since this occasions pain and is, of course, destructive of the very object it is intended to promote.

ARSENIC AND ZINC CHLORID.

ARSENI TRIOXIDUM.—U. S. P.—Arsenic Trioxid, also known as arsenous acid and as white arsenic; occurs most frequently as an odorless and tasteless white powder, that is but slowly soluble in about 100 parts of water.

ZINCI CHLORIDUM.—U. S. P.—Zinc Chlorid occurs as a white granular powder or a porcelain-

like mass. It is freely soluble in water, but the solution decomposes, on long standing or boiling, depositing a basic salt.

Arsenic and zinc chlorid have been used to destroy cancerous growths. Arsenic, particularly, has been widely used as the active constituent of various cancer cures that have been proposed by regular, as well as irregular, practitioners. Its action is very slow, and, therefore, it can be readily controlled, but it occasions considerable pain. Arsenic may be employed in the form of powder, as an ointment, either with lard or petrolatum, or as a paste. In the latter case the arsenic is suitably diluted with either starch or powdered althæa, and subsequently mixed with water to which a trace of gum or mucilage has been added. At present arsenic is frequently used for the destruction of the nerves in carious teeth.

Zinc chlorid is seldom used for its local corrosive action. It may be used in aqueous solution or fused on to suitable metallic instruments, much as silver nitrate is employed.

Mercuric chlorid is the most corrosive of the metallic salts, but it is too toxic to permit of its general employment for its local caustic action.

SOME OTHER OFFICIAL CAUSTICS.

ACIDUM NITRICUM.—U. S. P.—The official Nitric Acid contains 68 per cent. by weight, of absolute nitric acid, and occurs as a colorless, fuming liquid that is very caustic and corrosive.

LIQUOR HYDRARGYRI NITRATIS.—U. S. P.—Solution of Mercuric Nitrate occurs as a clear, nearly colorless liquid, having a faint odor of nitric acid and a strongly acid reaction. It should contain

about 60 per cent. of mercuric nitrate and about 11 per cent. of free nitric acid.

UNGUENTUM HYDRARGYRI NITRATIS.—U. S. P. —Ointment of Mercuric Nitrate is made by dissolving 7 parts of mercury in 10.5 parts of nitric acid and adding this solution to 76 parts of lard that has previously been partially decomposed by 7 parts of nitric acid, and continuing the heat, if necessary, until the reaction is completed. The resulting ointment should have a bright yellow color, whence its popular name, "citrine ointment."

UNGUENTUM HYDRARGYRI AMMONIATI.—U. S. P.—The Ointment of Ammoniated Mercury is now directed to be made by mixing 10 parts of ammoniated mercury with 50 parts of white petrolatum and 40 parts of hydrous wool fat.

CHROMII TRIOXIDUM.—U. S. P.—Chromium Trioxid, commonly called chromic acid, should be kept in glass stoppered bottles and great caution should be observed to avoid bringing it in contact with organic substances, such as cork, tannin, sugar alcohol, etc., as dangerous accidents might result because of its violent action as an oxidizing agent.

Nitric acid is a popular domestic remedy for the removal of warts. The surrounding surface should be thickly covered with petrolatum and a single drop at a time of the acid applied to the excrescence.

Solution of mercuric nitrate is sometimes used for chancres and where it is desired to destroy the tissue.

The ointment of mercuric nitrate is used more frequently than the solution; it is not so corrosive,

but is an active stimulant in syphilitic ulcers; it is also used in parasitic diseases of the skin. In the undiluted state it is too caustic for general use and is, therefore, usually diluted with lard. Ointment of ammoniated mercury is used in much the same conditions as the ointment of the mercuric nitrate. A 20 per cent. solution of chromium trioxid is sometimes used for the removal of warts as well as for condylomata. Its use is not without danger and it should not be applied to a large surface.

EMOLLIENTS.

The word emollient is derived from *emollio,* to soften; demulcent comes from *demulceo,* to smooth. Since the same agent is usually demulcent as well as emollient, the term to be used depends on the tissue to which the agent is to be applied, rather than on the medicinal agent itself. Mucous membranes rarely require softening, but an inflamed skin is frequently hard and rough, we therefore speak of applying demulcents to mucous membranes and emollients to the skin.

Not only bland oily substances and fats, but mucilages and diluted glycerin act as emollients. Glycerin, when diluted with water, and rubbed into the skin, prevents it from becoming dry and harsh, and the tendency to crack. Oils and fats penetrate the skin and render it soft.

SOME OFFICIAL EMOLLIENTS.

ADEPS LANÆ HYDROSUS.—U. S. P.—This preparation, formerly called lanolin, is the purified fat of the wool of sheep (*Ovis aries*), mixed with about 30 per cent. of water.

GLYCERINUM.—U. S. P.—Glycerin or glycerol is a clear colorless liquid of syrupy consistence, obtained by the decomposition of vegetable or animal fats. Anhydrous glycerin is slightly rubefacient, but when diluted it is, as previously stated, an efficient emollient.

MUCILAGO TRAGACANTHÆ.—U. S. P.—Mucilage of Tragacanth contains 6 per cent. of tragacanth and 18 per cent. of glycerin, with enough water to make 100 parts.

PETROLATUM.—U. S. P.—Under this general heading the present Pharmacopeia includes what was formerly known as hard and soft petrolatum.

Petrolatum, a mixture of hydrocarbons, of the methane series, is obtained from petroleum and should be of about the consistence of an ointment. The official substance may vary in color from yellow to light amber and have a melting point varying from 45° to 48° C. (113° to 118.4° F.). In addition to this, which is popularly known as yellow petrolatum, the Pharmacopeia also includes:

PETROLATUM ALBUM.—U. S. P.—This is a white unctuous mass, of about the consistence of ointment, that otherwise has the same chemical and physical characteristics as petrolatum.

PETROLATUM LIQUIDUM.—U. S. P.—Liquid Petrolatum is a colorless or only slightly yellowish, oily, transparent liquid without odor or taste, but giving off, when heated, a slight odor of petrolatum.

Of the vegetable oils that are useful as demulcents, it will suffice to enumerate:

OLEUM AMYGDALÆ EXPRESSUM.—U. S. P.—Expressed Oil of Almonds.

OLEUM GOSSYPII SEMINIS.—U. S. P.—Cotton Seed Oil.

OLEUM OLIVÆ.—U. S. P.—Olive Oil.

OLEUM THEOBROMATIS.—U. S. P.—Oil of Theobroma, so-called "cocoa" butter.

Of the several official preparations used as emollients, we may mention:

CERATUM.—U. S. P.—Cerate consists of 30 parts of white wax, 20 parts of white petrolatum and 50 parts of benzoinated lard.

UNGUENTUM.—U. S. P.—Ointment consists of 20 parts of white wax and 80 parts of benzoinated lard. These two preparations are used as emollients or as the bases for active medicinal substances.

LINIMENTUM CALCIS.—U. S. P.—Lime Liniment, or Carron oil, so called from the name of the iron works in England where this preparation had its origin, consists of equal parts of lime water and linseed oil. It has long been in use as a popular dressing for superficial burns and constitutes a readily applied and effective non-antiseptic remedy that rapidly allays the accompanying pain. If there has been extensive destruction of tissue, this remedy should be avoided, as it is not alone difficult to remove, but also forms a covering beneath which bacteria may proliferate safe from the reach of antiseptics.

UNGUENTUM AQUÆ ROSÆ.—U. S. P.—Ointment of Rose Water, or, as it is usually called, cold cream. This ointment consists of a mixture of spermaceti, white wax, expressed oil of almonds, sodium borate and rose water, and in one form or

another has been the most popular of the mild emollients from the time of its originator, Galen.

Emollients are used for the protection of inflamed skin against irritants, the choice depending on individual preference or convenience rather than on the nature of the drug. Thus mucilage of tragacanth, ointment of rose water and petrolatum differ widely in their physical properties, but they are all used for chapped hands, sunburn, and to soften the skin when it is rough and hard.

The bland oils and ointments penetrate the skin more readily than does diluted glycerin, and, therefore, they are to be preferred as emollients when they are also to serve as carriers of medicinal substances intended for absorption.

Diluted glycerin is an excellent agent for softening the skin, but is somewhat irritant, and when the sensitive layers of the skin are exposed, a bland oil or ointment, such as cold cream, is to be preferred.

To prevent chapping of the skin when it is exposed to the wind, to alternate wetting and drying, or to irritants, the mucilage of tragacanth, preferably mixed with an equal portion of glycerin, will be found useful. The exposed surface is washed with warm water and soap to soften the skin, and while it is still moist, but not wet, a little of the mucilage, or the mixture of mucilage and glycerin, is rubbed into the surface until the latter feels smooth. Instead of the tragacanth mixture the following may be preferred by some, but it is somewhat irritant to very delicate skin:

One ounce of glycerin soap is reduced to shavings and dissolved with the aid of gentle heat, in

half a pint of a mixture of equal parts of glycerin and water. This mixture solidifies on cooling, and a piece about twice the size of a pea is to be rubbed into the moist skin as often as may be necessary. Those who work with irritant or corrosive chemicals will find this an excellent agent for keeping the hands soft.

A liquid preparation that has met with considerable favor may be made by mixing ten parts of tincture of benzoin, fifty parts of water, and forty parts of glycerin. To secure a homogeneous mixture the water should be gradually added to the tincture of benzoin, and the glycerin added to this mixture. If the resulting mixture should still be irritating the amount of glycerin may be further reduced, with a corresponding increase in the quantity of the water. If rose water were substituted for the water in the above formula the resulting mixture would simulate some of the well-known and widely-advertised proprietary toilet preparations of glycerin and roses.

CHAPTER X.

LOCAL ANESTHETICS AND ANODYNES.

The introduction of cocain marked a decided advance in the production of local anesthesia.

Previous to that, freezing the part by immersion in a mixture of salt and snow, or shaved ice, or by spraying with ether or other volatile liquid, was used, and, while a procedure of this kind does produce complete anesthesia, the pain experienced during the freezing and thawing greatly exceeds that which would be caused by such a simple operation as opening an abscess or the removal of a small foreign body, such as a splinter or piece of glass, when readily accessible. It is because of the inherent dread which the average person has of the surgeon's knife, that he will undergo suffering akin to that with which he is familiar, rather than endure a lesser one which seems dreadful because it is unfamiliar.

It is also true that the injection of cocain sometimes causes more pain than would the operation for which it is given, and, since surgical operations have become so much more common than they were formerly, many adults willingly bear the brief, sharp pain of a simple incision, rather than resort to cocain, which has come into a certain disrepute because of the abuse of it by its victims, the majority of whom have become such through the use of supposedly harmless nostrums pretending to be

valuable remedies for hay fever and other minor affections.

Cocain, which is methyl-benzoyl-ecgonin, shows a certain chemical analogy to atropin and aconitin, which resemble it somewhat in their action on sensory nerves, and it is also related to phenol through the benzoyl group, since benzoic acid differs from phenol only by having a COOH group in place of the OH of the phenol. The anesthetic action of phenol is second only to that of cocain.

Aside from the systemic effect, which we need not fully detail here, cocain paralyzes sensory nerve endings with which it comes in contact and even nerve trunks when in sufficient concentration; if the solution is sufficiently dilute and the action not too long continued, the nerve endings rapidly return to normal (the nerve trunk more slowly), when the application is discontinued and the cocain removed by absorption into the general circulation, or evacuated.

It is denied that cocain has a specific action on the sensory nerve endings, their more exposed situation explaining the more prompt effect on them.

When a fairly strong solution (3 per cent.) is injected into the area about a nerve trunk, or an even weaker solution, 2 per cent., within the nerve sheath, both sensory and motor paralysis occur in about fifteen minutes, affecting, of course, the entire distribution of the nerve, the effect lasting for some hours after intraneural injection.

Since aqueous solutions are not absorbed from the unbroken skin, they must be injected beneath the epidermis, at least, in order that they may come into actual contact with the nerve ends.

When the solution is injected deeply into the muscular tissue the greater part of it passes into the general circulation and is lost so far as local action is concerned. To avoid this, it is better to inject the solution between the layers of the skin, at the same time limiting the circulation in the part as much as possible by compressing the blood vessels, preferably with a rubber band or other tight bandage.

Practically, the same object may be achieved by the use of a solution of the alkaloid of the suprarenal gland immediately preceding the injection of the solution of cocain. The injection of the solution of suprarenal alkaloid (epinephrin, adrenalin or one of the other trade preparations) causes a local vasoconstriction that in turn prevents the rapid absorption of the cocain solution into the general circulation, and also prevents, for the time being, the excessive hemorrhage that is so objectionable in minor operations. When it is necessary for the solution of cocain to diffuse through a part, a moment should elapse after the injection before applying the constricting bandage.

The combined use of suprarenal alkaloid and of cocain has proved to be of particular advantage in the eye and in the nose. One reason, and probably the most weighty one, is to be found in the fact that normal mucous surfaces have a tendency to absorb cocain very rapidly.

When cocain is applied to mucous membranes, either in powder or in solution, it causes its local effects for a short time and is then absorbed, producing its systemic action. Herein lies one of the chief sources of danger of the many so-called hay-

fever remedies, which virtually consist of cocain with some diluent powder, such as sugar of milk, and are intended to induce and to continue the truly terrible cocain habit.

Owing to the brief action and rapid absorption, frequent repetition is necessary to secure relief in "colds" and the user is peculiarly liable to become addicted to the habit which, in its baneful effects, is not exceeded, perhaps, in the whole range of drug addiction, not even excepting alcoholism. As a matter of fact, many of the so-called hay-fever nostrums are intended primarily for supplying those who are already victims of the habit and who would find difficulty in buying the drug under its correct name. This practice may be said to constitute a disgraceful example of the lack of proper control of the nefarious nostrum traffic by the law.

We should be particularly careful to warn patients and others against the insidiousness of this type of self-medication that our skirts may at least be kept clean in connection with this one phase of the evil.

Cocain in solution is readily decomposed on boiling, but if the solution be made with sterile, cold water there will be little cause to anticipate sepsis from its injection with the usual precautions. The solution may be sterilized, however, by heating to 80° C. (176° F.) for half an hour at a time on two successive days, care being taken to eliminate all possible contaminations of even a trace of alkali.

Eucain and stovain have the advantage of resisting decomposition by boiling, but, as just suggested, the disadvantage possessed by cocain is

more apparent than real, and the general action of cocain, particularly its possible complications, being well known, that drug, no doubt, will continue to hold first place as a local anesthetic, except where the ubiquitous detail man succeeds in frightening the more timid members of the profession into an exaggerated idea of the various dangers attending the proper use of the official article, and into a corresponding credulousness concerning the entire harmlessness of the particular substitute in which he is interested.

Cocain, when dropped into the eye, or taken internally, causes an incomplete dilatation of the pupil by stimulating the sympathetic nerve, reaction to light being maintained, differing therein from atropin, which abolishes this reflex.

OFFICIAL PREPARATIONS OF COCAIN.

COCAINÆ HYDROCHLORIDUM.—U. S. P.—Cocain Hydrochlorid, the most widely used preparation of cocain, is officially described as the neutral hydrochlorid of an alkaloid obtained from several varieties of coca. It occurs as colorless, transparent crystals or a white crystalline powder. It is soluble in less than one part of cold water and in 2.6 parts of alcohol, but is insoluble in petroleum benzin and in ether.

COCAIN.—U. S. P.—This is an alkaloid obtained from several varieties of coca, resembling cocain hydrochlorid in many of its properties, but being only slightly (1-600) soluble in water. It is soluble in 5 parts of alcohol and even more soluble in ether and in petroleum benzin. The alkaloid cocain is also soluble in about 12 parts of olive oil

and it, or the oleate, is to be used in making solutions of cocain in oil.

OLEATUM COCAINÆ.—U. S. P.—Oleate of Cocain contains 5 per cent. by weight of cocain in a mixture of oleic acid and olive oil.

The liquid preparations of coca, the fluid extract and the wine, are never used externally, although, if applied to the mucous surfaces, or to the abraded skin, their use would not be devoid of danger, from the absorption of the contained cocain, and other coca alkaloids.

Cocain is used locally on mucous membranes to allay irritation and inflammation as in hay fever, but it should be used very guardedly and not be too long continued. It is very much less useful in this condition than was formerly supposed and it has been very largely replaced by the now commonly used alkaloid of the suprarenal gland, which, it is claimed, allays the inflammation equally well and has the marked advantage of not inducing the habit.

Solution of cocain is very commonly injected hypodermically, to produce local anesthesia during such slight operations as the evacuation of abscesses, the removal of splinters, bullets, and other foreign bodies.

When there is considerable inflammation and extreme tenderness, stronger solutions are required than when a healthy surface is to be incised. In the former case, a syringe having a long, fine needle, is filled with a 4 per cent. solution of cocain hydrochlorid, the needle is then inserted obliquely, or almost parallel with the surface, between the layers of the skin, beyond the zone of

increased tenderness, and a small drop of solution is forced beneath the epidermis; a white spot is seen in a moment and the needle is then advanced through that toward the more tender area without removing the point of the needle from beneath the epidermis; with each advance a drop of the solution is injected. When the needle has been passed under the epidermis for its full length, it is withdrawn and the point inserted into the most advanced blanched area; in this way, using a curved needle, a complete circuit may be made of the seat of inflammation. The object of injecting the solution between the layers of the skin is to secure anesthesia with a minimum of absorption into the general circulation.

The psychic effect on the patient of having painless injections made into such an extremely tender region tends to allay the nervous dread of the knife, which is a more important factor than we, who are accustomed to seeing pain, are apt to realize.

The injection of a solution of cocain into the hand is apt to prove ineffective when the trouble is deep seated, as in palmar abscess, and in such cases it is better to inject a small amount of a 2 or 3 per cent. solution around or into the nerve trunks in the forearm.

The injection of strong solutions into nerve trunks has given rise to much trouble and it is preferable, therefore, to try to secure the effects from weak solutions.

Kast and Meltzer have very recently shown that the abdominal organs are capable of exhibiting sensations of pain, and that these sensations are

increased by inflammation, but that they may be completely abolished by a subcutaneous injection of cocain.

Anesthesia involving all the body below the site of the injection may be secured by injecting about ten or fifteen minims of a 2 per cent. solution of cocain hydrochlorid into the subarachnoid cavity through a sterilized platinum needle which is inserted at the side of the fourth lumbar vertebra. The patient must be placed in a sitting position, in order that gravity may not favor the passage of the solution up to the medulla.

This method of using cocain (or any other drug) is attended with so much danger that it is not justifiable except when, for some reason, general anesthesia is not practicable.

The anesthesia is induced in ten or fifteen minutes, with cocain, but its duration is very variable, lasting from half an hour to five hours.

When the application of a constricting band is not feasible the previous injection of a solution of the suprarenal gland, as previously suggested, will delay the absorption of the solution of cocain into the general circulation. It should be remembered, however, that the use of a vasoconstrictor only delays and does not prevent the absorption of the cocain. When a large amount of the cocain solution is necessary it will probably be preferable to use the infiltration method as proposed by Schleich. It is difficult to see what advantage is to be gained by the addition of morphin to a solution instead of directing the injection of the desired amount at once so as to secure its sys-

temic effect. Schleich recommended solutions containing from 0.01 gm. (1/6 grain) to 0.2 gm. (3 grains) of cocain hydrochlorid and from 0.005 gm. (1/12 grain) to 0.25 gm. (½ grain) of morphin hydrochlorid in 100 c.c. (3 fluid ounces) of 0.2 of 1 per cent. solution of sodium chlorid to which was added one-fourth of a drop of phenol.

Strong solutions of cocain should not be used in carious teeth, and only small amounts of the weak solution. One or two drops of a 1 per cent. solution often affords relief from toothache.

Cocain is sometimes applied to hemorrhoids to lessen the pain and it may be said that its local use is much more rational than is that of opium, since the alkaloid morphin has no local analgesic or vasoconstrictor action, a fact to be remembered when prescribing urethral injections, and lotions for inflamed surfaces of the skin.

Cocain has also been used, in small doses, to relieve nausea. It may be given alone or with other antiemetics. The following is an example of a combination with cerium oxalate, the latter being used empirically:

℞.	Cocainæ hydrochloridi.....gr. i	0	06
	Cerri oxalatis.....gr. xvi	1	
	Aquæ aurant. flor.....f℥i	30	

M. Sig.: Shake the mixture and give one teaspoonful every half hour when needed.

Many substitutes for cocain, of greater or less merit, have been brought forward by manufacturers, and, while they have been widely heralded as being superior to cocain, they are not free from disadvantages; though the manufacturers have not, as yet, devoted much time or space to the

exploitation of these several disadvantages or dangers. Their further consideration, however, does not belong in a treatise on the Pharmacopeia.

Hydrocyanic acid is a general protoplasmic poison rapidly causing paralysis and death to any tissue to which it is applied. It induces anesthesia when applied to mucous membranes, but owing to its rapid absorption and extreme toxicity it is not well suited for the purpose, though it is occasionally employed to depress the sensory endings when dyspepsia is attended with pain in the stomach. Death occurs so quickly from fatal doses, owing to the rapidity of absorption from the mouth and stomach, that there is rarely a chance for medical interference. It causes paralysis of the heart and respiration; hence artificial respiration is of no avail in the majority of cases, but if the dose has been insufficient to paralyze the heart strychnin may be used as a respiratory stimulant. Sodium hyposulphite is said to be useful as a chemic antidote, since it forms the sulphocyanid. From 2 to 4 drams (8 to 16 grams) of the hyposulphite dissolved in water is directed to be injected subcutaneously.

ACIDUM HYDROCYANICUM DILUTUM.—U. S. P. —Diluted Hydrocyanic Acid contains 2 per cent. of absolute hydrocyanic acid. As found in the shops it is of variable strength, owing to its tendency to decompose.

Dilute hydrocyanic acid is sometimes used on the *unbroken* skin to allay itching, and it may be used internally with extreme caution to prevent the vomiting of pregnancy.

THE ATROPIN GROUP.

Atropin, which will be mentioned among the analgesics, acts locally as an anesthetic, its effects resembling those of cocain, but being weaker.

ATROPINA.—U. S. P.—Atropin is officially described as an alkaloid obtained from *Atropa Belladonna* and from other plants of the same family. As it occurs in commerce, it is usually contaminated by a small amount of hyoscyamin, from which it can not be readily separated.

Atropin is soluble in 450 parts of water and in 1.5 parts of alcohol. It is very poisonous, the average dose being 0.0004 gm. (1/160 grain), and it should, therefore, be tasted with the utmost caution and only in dilute solution.

ATROPINÆ SULPHAS.—U. S. P.—This is the sulphate of the alkaloid atropin. In its physiologic properties and dose, atropin sulphate corresponds closely to atropin. It is soluble in less than one part of water and in about four parts of alcohol.

OLEATUM ATROPINÆ.—U. S. P.—Oleate of Atropin is a mixture of equal parts of oleic acid and olive oil, containing 2 per cent. of atropin, in solution.

EXTRACTUM BELLADONNÆ FOLIORUM.—U. S. P.—Extract of Belladonna Leaves is directed to be made with a menstruum consisting of two parts of alcohol and one part of water, and should contain, when assayed according to the process given in the Pharmacopeia, 1.4 per cent. of mydriatic alkaloids.

UNGUENTUM BELLADONNÆ.—U. S. P.—Belladonna Ointment contains 10 per cent. of extract of

belladonna leaves in a mixture of hydrous wool fat and benzoinated lard.

EMPLASTRUM BELLADONNÆ.—U. S. P.—Belladonna Plaster is now directed to be made by mixing 30 parts of extract of belladonna leaves with 70 parts of adhesive plaster, and corresponds closely with the widely used, commercial, rubber-base plasters. It is further directed that spread belladonna plasters should yield, when assayed by the process given in the Pharmacopeia, not less than 0.38 nor more than 0.42 per cent. of mydriatic alkaloids.

FLUIDEXTRACTUM BELLADONNÆ RADICIS.—U. S. P.—Fluidextract of Belladonna Root is directed to be made with a mixture containing four parts of alcohol and one part of water, and should yield, when assayed by the process given in the Pharmacopeia, 0.5 per cent. of mydriatic alkaloids from belladonna root.

LINIMENTUM BELLADONNÆ—U. S. P.—Belladonna Liniment is virtually a solution of five parts of camphor in a sufficient quantity of fluidextract of belladonna to make 100 parts.

FLUIDEXTRACTUM STRAMONII.—U. S. P.—This is directed to be made from the leaves of *Datura Stramonium* with a menstruum containing two parts of alcohol and one part of water. The finished fluidextract is required to contain 0.35 per cent. of the mydriatic alkaloids from stramonium.

EXTRACTUM STRAMONII.—U. S. P.—Extract of Stramonium is made by evaporating the fluidextract to the required consistency, and should contain 14 per cent. of mydriatic alkaloids.

UNGUENTUM STRAMONII.—U. S. P.—Stramonium Ointment contains 10 per cent. of extract of stramonium in a mixture of hydrous wool fat and benzoinated lard.

Atropin, in this form of an ointment or the oleate, and the extracts of belladonna and of stramonium, in the form of ointments, belladonna plaster and belladonna liniment are very commonly employed as local applications for the relief of the various neuralgias. The members of the atropin group are said to be more efficacious in facial than in other neuralgias, but they are also used for the intercostal variety and for lumbago.

Atropin is sometimes employed locally to prevent sweating, but it is of doubtful value for this purpose.

Belladonna plasters are very commonly used, particularly by the laity, for a variety of pains, often serving merely to protect the surface, or for the retention of body heat. They slowly induce a diminished sensitiveness in the surface to which they are applied, and occasionally they give rise to toxic symptoms.

Suppositories of extract of belladonna are frequently used with benefit in the treatment of hemorrhoids.

They may be directed somewhat as follows:

℞. Extracti belladonnæ fol.....gr. i |06
Olei theobromatis .....ʒii 8|
M. Ft. suppositoria No. viii.
Sig.: One every four hours, as directed.

Belladonna ointment may be used for the same purpose. It may be directed to be spread on a little cotton which is placed in contact with the piles and they are then replaced in the rectum. If

they still tend to protrude a pad of cotton is placed over the anus and held in position by a bandage. For men the bandage may be attached to the suspenders, both back and front, when the severity of the attack is not such as to compel the patients to lie down.

It must be remembered that the extract of belladonna, whether applied as a suppository or ointment, is rapidly absorbed and the amount so used must not exceed the therapeutic dose.

ACONITE.

Aconite owes its action almost entirely to aconitin, an alkaloid which, like cocain, is composed of a base united to an aromatic acid. Closely resembling aconitin in its local action is veratrin. They both cause irritation when applied to the mucous membrane.

The effect of aconitin when taken by the mouth is very characteristic, the local effect being a tingling and then a disagreeable sensation in the throat which has been variously termed itching or "scratching." Applied to the skin, aconitin causes sensory stimulation, which is succeeded by local anesthesia without the production of rubefaction.

Aconitin is much less efficacious than cocain as a local anesthetic, and, of course, its injection is wholly inadmissible, but it is much more useful in the form of a liniment which is to be applied to the unbroken skin, through which aconitin may penetrate to a slight extent.

ACONITINA.—U. S. P.—An alkaloid obtained from the official aconite, the tuberous root of *Aconitum napellus.* There are a number of close-

ly related species of aconite that contain alkaloids which differ widely in their physiologic action and dose. The now official aconitin is the purified crystalline alkaloid of the official root and should not be confounded with the amorphous alkaloid formerly official or with any one of the more potent alkaloids obtained from other species of aconite.

Aconitin is soluble in 3,200 parts of water and in 22 parts of alcohol. On account of the poisonous character of this alkaloid, it should never be tasted, except when in very dilute solution.

Average dose: 0.00015 gm. (0.15 mg. or 1/400 grain).

FLUIDEXTRACTUM ACONITI.—U. S. P.—Fluid-extract of Aconite is directed to be made from the powdered root of *Aconitum napellus* with a menstruum composed of three parts of alcohol and one part of water. It should contain no less than 0.4 per cent. of aconitin.

TINCTURA ACONITI.—U. S. P.—This tincture now represents 10 parts of the crude drug, instead of 35 parts, as formerly official. It is made with a menstruum containing 7 parts of alcohol and 3 parts of water, and the finished tincture should contain 0.045 per cent. of aconitin.

VERATRIN.

Somewhat closely related to aconitin, in its various properties and uses, is veratrin, which is official in several well-known forms.

VERATRINA.—U. S. P.—The official Veratrin is a mixture of alkaloids obtained from the seeds of *Asagræa officinalis.* It occurs as a white or a grayish-white amorphous powder that is soluble in

about 1,750 parts of water and in 2.2 parts of alcohol.

OLEATUM VERATRINÆ.—U. S. P.—Oleate of Veratrin contains 2 per cent. of veratrin in a mixture of equal parts of oleic acid and olive oil.

UNGUENTUM VERATRINÆ.—U. S. P.—Veratrin Ointment contains 4 parts of veratrin with 6 parts of expressed oil of almonds and 90 parts of benzoinated lard.

LOCAL USES OF ACONITIN.

Aconitin is sometimes used locally in the form of an ointment (from 1 to 100 to 1 to 500), or in the form of an oleate, made similarly to the official oleates of atropin or of veratrin, of 2 per cent. strength, for the relief of rheumatism and neuralgia. Inasmuch as it is absorbed in these forms from the unbroken skin, and much more rapidly from wounds or mucous membranes, it must be used with caution.

For facial neuralgia it may be prescribed as follows:

℞. Aconitini .....gr. iii | 20
Alcohol q. s. to dissolve
Adipis .....ʒiv | 15
M. Ft. unguentum.
Sig.: Apply a very little of the ointment over the seat of the pain.

The fluidextract of aconite may be further concentrated and used in the form of an ointment, or it or the tincture of aconite may be used as a liniment, applied on cloth, and a hot pad or water bottle laid over the surface.

For muscular rheumatism a liniment composed of equal parts of the tincture, or a corresponding

amount of the fluidextract and soap liniment may be rubbed on the surface, or, if desired, this liniment may be further varied by the addition of chloroform liniment, or other alcohol soluble rubefacient in place of the soap liniment.

The following is the formula recommended by Magitot for toothache:

℞.	Tincturæ aconiti	
	Chloroformi, āā.....m. xlv	3
	Tincturæ benzoini.....m. cl	10
M.	Sig.: Apply as needed.	

PHENOL.

Phenol, or carbolic acid, has been considered under the subject of antiseptics.

Applied to the skin, pure or in concentrated solution, it causes tingling and some pain, with the formation of a white eschar and a rapidly induced partial or complete anesthesia of the part. It is so prone to absorption when weak solutions are used that its usefulness is interfered with to a great extent.

Phenol, in 2 to 3 per cent. solution, applied for a short time only, causes wrinkling, with a lessening of sensibility and of the secretion of sweat, but solutions even as weak as 3 per cent., applied for some hours to an extremity, for instance to the finger, may give rise to gangrene resembling that seen in ergotism. Kobert states that this has been reported in no less than 50 cases in the past few years.

PHENOL.—U. S. P.—The Acidum Carbolicum of former pharmacopeias, occurs as separate needle-shaped crystals or as a white crystalline mass that is soluble in about 20 parts of water, but

is freely soluble in alcohol, glycerin or in fixed or volatile oils. Phenol will absorb or dissolve from 15 to 20 per cent. of water, and then occurs as a colorless or slightly reddish liquid.

If a solution of phenol stronger than 5 per cent. is desired, the phenol should be added to an equal volume of glycerin and the mixture diluted to the required degree. Failure to observe this precaution has resulted seriously, owing to the separation of phenol from the solution.

PHENOL LIQUEFACTUM.—U. S. P.—Liquefied Phenol should contain not less than 86.5 per cent. by weight of absolute phenol and about 13.6 per cent. by weight of water.

GLYCERITUM PHENOLIS.—U. S. P.—Glycerite of Phenol consists of 20 parts of liquefied phenol and 80 parts of glycerin, by measure.

UNGUENTUM PHENOLIS.—U. S. P.—Ointment of Phenol is now directed to contain 3 per cent. of phenol, in white petrolatum.

Phenol is occasionally used for the production of anesthesia preliminary to incising the skin, and, in the form of the glycerite, or preferably the ointment, it is very useful in allaying the pain of small ulcers and burns. It may momentarily increase the pain, but this is soon followed by lessened sensibility.

It is, of course, obvious that the use of phenol is not permissible where large surfaces are to be treated.

When antisepsis is not of especial importance the ointment is to be preferred, as the continuous application of even comparatively weak aqueous solutions to the extremities has caused gangrene.

CHAPTER XI.

GENERAL ANESTHETICS.

The subject of general anesthesia concerns the surgeon much more than it does the physician, but, as in the matter of antisepsis, the physician must have some knowledge of this subject, and we shall, therefore, briefly consider the more important members of the group of general anesthetics, their uses and their probable limitations.

Narcotics have been used from time immemorial, for producing unconsciousness during surgical operations, but nitrous oxid has been in use longer than any other agent now employed for inducing general anesthesia. It is more than 100 years since Sir Humphrey Davy first suggested this use for nitrous oxid after observing its effects on himself while he was suffering with toothache, but his suggestions met with no response, and it was not until many years later, in 1844, that Horace Wells, a dentist of Hartford, Conn., employed it for that purpose and thus introduced what he was pleased to term "a new era in tooth-pulling."

It was at one time supposed that nitrous oxid caused unconsciousness merely through asphyxia, and, while this is a very important factor, it has been shown that nitrous oxid also causes a depression of the central nervous system resembling that of the methane derivatives, such as chloroform and ether, and complete anesthesia has been produced without asphyxia by using a mixture of oxygen

and nitrous oxid under pressure. This would probably constitute an ideal method of inducing anesthesia were it not for the mechanical difficulties and the expense that it necessarily involves.

Nitrous oxid is usually administered only for a short time, it being necessary to discontinue it so soon as marked cyanosis of the face occurs, after which the anesthesia lasts for about a minute or two. It is the safest agent which we possess for general anesthesia, the death rate being approximately one in half a million cases, but, aside from its use in dentistry and for inducing unconsciousness preliminary to other anesthetics, its application is extremely limited.

In the larger hospitals of New York, ether anesthesia is now systematically preceded by nitrous oxid or ethyl chlorid.

It is impossible to estimate the value to mankind, and to surgery in particular, of the introduction of anesthetization with ether by Morton and Jackson some fifty years ago. Its use by Dr. Crawford W. Long, in Georgia, antedates by more than two years the real work of Morton and Jackson in introducing the method, but the greatest credit is due those men for their splendid achievement in gaining general recognition for this boon to humanity.

Shortly after the introduction of general anesthesia by the use of ether Sir J. Y. Simpson announced his discovery of the use of chloroform as an anesthetic, and this latter agent soon displaced ether almost entirely in many parts of the world. Even at present chloroform is used almost exclusively in several European countries.

From time to time other agents have been proposed as substitutes for chloroform and ether, and some of them have enjoyed a greater or less popularity for a time, only to sink into obscurity.

In this connection we may mention a few of those which will be remembered even by the younger generation of physicians, and which have not yet fallen into complete disuse.

Ethyl bromid and bromoform have been used to some extent as general anesthetics, and it has been suggested that the typical bromid action might be obtained from them, but the action is that of the entire molecule. Both of these have passed almost completely from use as general anesthetics, largely, perhaps, because of the unstable character of the substances themselves and the accompanying uncertainty of the action of the decomposition products.

Petroleum ether, or benzin, because of its cheapness, is sometimes used in vivisection experiments, but not on man.

The use of mixtures of varying composition appears to offer a peculiarly interesting field for experimentation in connection with general anesthesia.

Of the several mixtures that have been used from time to time, that popularly known as the A. C. E. mixture, containing 1 part of alcohol, 2 parts of chloroform and 3 parts of ether, is perhaps the one that has been used most widely. This, also referred to occasionally as the one-two-three mixture, was, at one time at least, quite popular in England. While it has been urged against this mixture that the differences in volatility of the

three substances prevent the anesthetist knowing just what he is administering, it is a fact that the vapors of all three tend to pass off together, and, furthermore, the object is to induce anesthesia and to avoid an excess of the anesthetic and the action of the mixture seems to be as easily controlled as that of chloroform, while not so much is required as of ether alone. The alcohol and chloroform raise the boiling point of the mixture above the temperature of the lungs, and this probably secures some of the advantages claimed by Schleich for the mixture of ether, chloroform and benzin.

A mixture containing 57 parts of ether and 43 parts of chloroform has been suggested as having some advantages over either of its component parts. It was at one time quite widely recommended under the title of M. S. mixture, but appears to have fallen into disuse, having probably no advantage over the better known A. C. E. mixture mentioned above.

Dr. Carl Ludwig Schleich of Berlin some years ago recommended the admixture of 5 per cent. of petroleum ether, or benzin, with ether and chloroform, as a general anesthetic. This preparation had been used by Schleich in nearly 500 cases in which he obtained excellent results, such as absence of excitement and of the excessive salivary discharge so frequently seen with ether, while the depressing effect of the chloroform on the heart was not observed. Despite these and other advantages, which he cited at the time, the mixture never attained much popularity, and even Schleich himself appears to have discontinued its use in favor of an ethyl chlorid mixture.

The mixture of ether, chloroform and ethyl chlorid has been proposed at different times and in varying proportions; the one proposed by Schleich contains 2 parts of ethyl chlorid, 4 parts of chloroform and 12 parts of ether, and is fairly representative of this class.

The advisability of using mixtures of any kind, for general anesthesia, is still an open question, particularly in view of the fact that the several chemical substances themselves are far from being absolutely stable, even under the most favorable conditions, chloroform particularly being readily decomposed and forming, as one of the possible decomposition products, the really dangerous substance known as phosgene.

MAGNESIUM SULPHATE.

S. J. Meltzer has recently suggested the use of a solution of magnesium sulphate for inducing general anesthesia. For this purpose he advised the intraspinal injection of 1 c.c. (15 minims) of a 25 per cent. sterilized solution of magnesium sulphate for each 25 pounds of body weight. This method possesses no advantage over cocain used in the same way for producing anesthesia of the lower parts of the body, but general anesthesia is induced and persists for some hours, and the method, therefore, may possibly prove serviceable in controlling the convulsions of tetanus.

Marked depression of the respiration occurs, and it must be used only with extreme caution. The sudden introduction of a small quantity of this solution into the blood vessels will immediately prove fatal.

SCOPOLAMIN-MORPHIN AND SIMILAR SOLUTIONS.

The constant search for less dangerous anesthetics than ether and chloroform brings many substances into notice. Morphin and scopolamin have found an ardent champion in Korff, who has used them for several years. He employs up to 0.035 gm. (½ grain) of morphin and 0.0013 gm. (1/45 grain) of scopolamin. Unconsciousness does not occur, and he claims absolute quiet must be maintained, while he stops operating long enough for pain to subside. He advises "drops" of chloroform or ether when necessary. The tongue must not be permitted to fall back into the throat. The use of this method of anesthesia in major surgery must obviously be very limited. A discussion of a number of fatalities attending the use of morphin and scopolamin for general anesthesia will be found in *La Semaine Medicale,* Nov. 8, 1905, p. 529, and in THE JOURNAL of the American Medical Association during 1906 and 1907.

The combination of scopolamin and morphin may have certain advantages in obstetrics, but it is of the utmost importance that the proper technic be observed. Gauss has elaborated a method most carefully, and those who employ the combination will do well to read his article in the *Centralblatt für Gyn.,* Jan. 12, 1907. Other authorities condemn the practice on the grounds that it is harmful to mother and child without accomplishing the desired results.

In view of the known dangers attending the use of scopolamin and morphin we must view the statements of those who are financially interested in the sale of this combination with extreme sus-

picion. It can not be stated too emphatically that cactin adds nothing whatsoever to the safety of this combination.

Morphin sulphate alone or in combination with atropin sulphate is very commonly employed preliminary to chloroform or ether narcosis, and appears to have well-established uses in this connection.

E. Fraenkel reported some ten years ago that he had habitually used a mixture of morphin, atropin and chloral for hypodermic injections, preliminary to narcosis, for twenty-two years, without an accident. He claimed that this procedure lessened to an extraordinary degree the amount of chloroform or ether used to maintain anesthesia.

The solution used by Fraenkel was made as follows:

Morphin muriate	gr. iiss		15
Atropin sulphate	gr. ¼		015
Hydrated chloral	gr. iv		25
Distilled water	℥ss	15	

He injected hypodermically from 1 c.c. to 1.25 c.c. (15 to 19 minims) fifteen minutes before the commencement of the ether or chloroform administration.

Fraenkel further asserts that this mixture is free from the objectionable side actions of morphin, being well borne by patients who could not take morphin by the mouth or hypodermically.

ETHYL CHLORID.

A substance which bids fair to rival chloroform and ether as a general anesthetic, under certain conditions at least, is ethyl chlorid.

This substance is extremely volatile, boiling at from 12° to 13° C. (53.6° to 55.4° F.), and it is necessary, therefore, to keep it in sealed tubes. The ends of the tubes are drawn out to fine capillary tubes which are then sealed, or the capillary opening is closed by a metal cap which may be replaced when a part of the contents of the tube has been used. When required for use the glass tip is broken off, or the metal cap unscrewed, when the heat of the hand causes the ethyl chlorid to volatilize, forcing out a fine stream which may be directed against the surface which is to be frozen for local anesthesia, or the stream may supply the vapor for inhalation to produce general anesthesia.

Ethyl chlorid induces anesthesia more rapidly than ether does, and when it is withdrawn the patient recovers more quickly, thus saving an average of some twelve minutes on each operation, hence it is likely to prove useful on the battlefield and in great calamities when a number of operations must be performed with a minimum loss of time.

Figures purporting to give relative degrees of danger for various anesthetics are notoriously unreliable, but it seems probable that ethyl chlorid is less dangerous than chloroform and somewhat more dangerous than ether. Among the objectionable features of ethyl chlorid are increased cost, the explosive character of the vapor, extreme volatility, the accompanying waste of material and the difficulty of maintaining anesthesia.

A number of masks have been devised for use with ethyl chlorid. It has been suggested that the mask should be so arranged that the anesthetic does not come too near the face, as freezing may

thus ensue. Ethyl chlorid appears to be especially adapted for short operations, and in some hospitals it is replacing nitrous oxid preliminary to ether anesthesia.

ACTION OF CHLOROFORM AND ETHER.

It would hardly be profitable to discuss here in detail the actions of chloroform and ether, but there are certain important points concerning them which are so frequently overlooked that we will consider them briefly.

While there are records of as many as 40,000 consecutive anesthetizations with chloroform without a fatality, this is only possible in case of skilled anesthetists working with carefully selected cases. Certainly no such results are possible in ordinary practice, and with that alone we are concerned at present.

We must always remember that the production of general anesthesia is a grave matter, in which death is an ever-present possibility despite the utmost care, and of which there is actual danger unless caution is observed. The possibility of fatal complications in all cases of general anesthesia would appear to make it necessary that the patient or his friends be informed of this fact, if for no other reason than to protect the physician administering the anesthetic.

Each case must be carefully considered when selecting the anesthetic, and neither chloroform nor ether should be used exclusively. Ether being the safer, however, should have the preference, when it is not contraindicted, and chloroform should not be used unless the anesthetist is experienced and is reasonably skilled in the use of it.

The following are some of the principal advantages and contraindications of both of these agents:

The vapor of ether is inflammable, that of chloroform is not, and the latter is to be preferred when operations are to be performed by gas or lamplight. In this connection, however, we must not forget that chloroform vapor coming in contact with an open flame is readily decomposed into chlorin and hydrochloric acid, and that it will be necessary, therefore, to provide for free ventilation to eliminate these decomposition products. If ether must be used under such circumstances, the light should be placed as high above the level of the mask as practicable, since ether vapor is heavier than air. The thermocautery can, of course, also ignite the vapor of ether.

An acute cold is a contraindication to the use of any anesthetic, but more particularly to the use of ether. Ether is also contraindicted in bronchitis, because of the great irritation caused by the relatively large amount necessary to maintain anesthesia; it is likewise contraindicated in nephritis, since the kidneys take part in the excretion, and suffer from the irritant action.

In extremely hot weather, that is, when the thermometer is above 93° to 95° F. (34° to 35° C.), ether is volatilized so rapidly that the atmosphere contains amounts which may prove objectionable, and it often becomes very difficult to maintain complete anesthesia.

When it is absolutely imperative to reduce the stage of excitement to the minimum, or when it becomes necessary to secure complete anesthesia rapidly, ether is contraindicated and chloroform is

to be preferred when it is not specifically contraindicated for other and more important reasons. In the latter event ethyl chlorid may be used, or preliminary unconsciousness may be induced by nitrous oxid, and this followed up by the use of ether.

Chloroform is very commonly preferred by obstetricians, but deep anesthesia is not usually induced in such cases.

In fatty disease of the heart chloroform is contraindicated because it also induces fatty degeneration of that organ; and for this reason it is not advisable to use it repeatedly on the same person in succeeding operations.

Chloroform is much more toxic to the heart than ether, and there is a much narrower margin for safety between the amount necessary to induce anesthesia and that which causes death, chloroform being much more active than ether in inducing anesthesia, but very much more toxic.

A matter of the greatest importance, especially for the unskilled anesthetist, is the very brief interval between the cessation of respiration and the stopping of the heart beat with chloroform, giving very little chance to resuscitate the patient after respiration has stopped. With ether the interval is much longer, and the prompt resort to artificial respiration, while the body is raised higher than the head, very commonly results in saving the patient.

This difference in the action of anesthetics and also the fact that the condition of anesthesia is a dangerous one, according to the degree to which it is carried, will be more fully appreciated if we

have a clear conception of the several stages of anesthesia and the rapidity with which a patient may pass from one stage into the other.

These several stages are usually designated as: 1, the stage of excitement; 2, the narcotic and anodyne stage; 3, complete anesthesia; 4, paralysis and death.

The acceleration of the circulation noticed in the first stage is similar to that produced by the ingestion of alcohol or alcoholic beverages, and the production of this stage was one of the uses to which ether was put long before it was used as an anesthetic in surgical operations. From this stage the patient usually passes quite gradually into the second or narcotic stage.

In the narcotic stage sensibility becomes impaired, but there is not infrequently a persistence of reflex action which manifests itself in a form of delirium or wild excitement. This is usually an indication of faulty anesthetization and is a complication that can be avoided in many instances by the more careful preparation of the patient for the anesthetic. In the majority of instances, however, the patient passes rapidly into the third stage, that of complete anesthesia. In this stage there is complete absence of reflex action, even of the conjunctiva, which is usually, though erroneously, advocated as the most satisfactory test for complete anesthesia. A satisfactory surgical anesthesia is indicated by complete relaxation of nearly all of the muscles of the body, regular breathing, deep inspirations and a fully relaxed lower jaw. The widely prevailing though barbarous habit of

touching the conjunctiva should never be resorted to.

By the careful administration of the anesthetic this stage of surgical anesthesia may be continued for a considerable period of time, but we must never forget that it is ever bordering on, and may at any moment pass into, the fourth or paralytic stage, when respiration ceases, the heart beats become feebler, and, unless vigorous and prompt restorative measures can be resorted to, may cease entirely.

THE ADMINISTRATION OF ETHER.

While it has been asserted that the administration of anesthetics is an art that can not be taught or learned, but must be acquired, it is also true that there are certain points or rules that have been sufficiently well established to warrant their being heeded, and the general conduct of anesthetization can best be illustrated, perhaps, by giving the method pursued by an ordinarily careful anesthetist, when nitrous oxid is not used.

The patient, who should not have had food for five hours preceding, is made thoroughly comfortable, in a recumbent position, on a table or wheel stretcher, if in a hospital, with a pillow just sufficient to raise his head but slightly.

The mouth is freed from false teeth and other foreign materials, and the lips and nose are anointed with petrolatum to avoid the accompanying irritation from contact with the anesthetic.

A pad of moistened gauze is then placed over the eyes to avoid irritation by the fumes of the anesthetic.

All these several stages should be carefully explained to the patient so as to assure him that every possible precaution is being taken to provide for his comfort and well-being, and to gain his confidence, for the more important feature of administering the anesthetic itself.

After the patient has been prepared and his confidence gained by explanation of the several stages of the preparation, he is allowed to accustom himself somewhat gradually to the taste and smell of ether. To accomplish this the cone or gauze containing the anesthetic is held some slight distance from his face, and gradually brought closer as the patient becomes more and more accustomed to the inhalation. If the anesthetist has been successful in gaining the confidence of the patient he will find that the latter will pass through the preliminary stages of anesthesia without a struggle, and that complete relaxation will be secured with a minimum of the anesthetic.

When a patient has been completely anesthetized less of the anesthetic will suffice to maintain the condition and the further efforts of the anesthetist can be devoted to observing the respiration and the surface reflexes of the patient in order to prevent his reverting to the second stage of anesthesia, or passing on into the much-to-be-dreaded stage of paralysis of the respiratory center.

With chloroform the passing from one stage of anesthesia to the next is much more rapid than with ether, less of the anesthetic is used, more air must be allowed, and there is, of course, a correspondingly smaller margin of safety in the stage of complete surgical anesthesia.

Since all of us can not become expert anesthetists and yet must at times perform that office, this advantage of ether is well worth consideration.

The greatest immediate danger from inhalation of ether or chloroform, but more especially of the latter, is the administration of the vapor in too great concentration. One hundred volumes of air require approximately from three to four volumes of ether vapor, and 100 volumes of air require about one volume of the vapor of chloroform to induce anesthesia, but an increase of from two to three volumes in the concentration of the ether, or of only one volume of chloroform in 200 of air will prove fatal in a short time.

While we do not actually measure the relative volumes of air and vapor, as a rule, these figures will serve to show the comparative danger of the two substances, for it is many times more difficult to avoid overstepping narrow boundaries than broad ones.

When a perfectly safe ratio is maintained the delay in inducing anesthesia often proves vexatious, and the anesthetist may be urged to expedite the operation by increasing the concentration, but he should never forget the grave responsibility which he has assumed and should never permit the impatience of others to induce him to exceed the limits of caution, save only in those grave emergencies where delay in operating may mean death to others who are awaiting their turn.

OFFICIAL ANESTHETICS.

ÆTHYLIS CHLORIDUM.—U. S. P.—Ethyl chlorid occurs as a colorless, transparent, very vol-

atile liquid, having a characteristic, rather agreeable odor and a burning taste. It is only slightly soluble in water, but is readily miscible with alcohol.

Ethyl chlorid is a haloid derivative, and is prepared by the action of hydrochloric acid gas on absolute ethyl alcohol. It is usually marketed in hermetically sealed glass tubes, and when liberated at ordinary room temperature volatilizes almost instantly. The resulting gas is very inflammable and the substance itself should never be used in proximity to an open flame or fire.

For local anesthesia the liquid in a fine spray is applied to the surface to be anesthetized.

The average amount necessary to induce general anesthesia is from 5 to 10 c.c. (75 to 150 minims).

ÆTHER.—U. S. P.—Ether is a transparent, colorless, volatile liquid having a characteristic odor and a pungent, sweetish taste. It should contain 96 per cent. by weight of absolute ether or ethyl oxid and about 4 per cent. of alcohol containing a little water.

The per cent. content of ethyl oxid or absolute ether in a given specimen is a matter of considerable importance when the substance is to be used for anesthesia. The official ether, when exposed to air, absorbs moisture, thus materially reducing the anesthetic value of the ether. The practice that has long been followed of sending out ether in hermetically sealed cans is an efficient safeguard against this absorption of moisture.

CHLOROFORMUM.—U. S. P.—Chloroform is a heavy, clear, colorless liquid having a characteristic ethereal odor and a burning, sweet taste. It should

contain not less than 99 per cent. by weight of absolute chloroform and from 0.6 to 1 per cent. by weight of alcohol.

Chloroform when not pure is readily decomposed, forming chlorin compounds that may prove to be extremely dangerous to the patient. Even chloroform that corresponds to the requirements of the Pharmacopeia may be decomposed in the presence of damp air and heat, and the substance should, therefore, be carefully preserved in small, well-stoppered bottles.

CHAPTER XII.

EXPECTORANTS.

The expectorants official in the United States Pharmacopeia afford a great variety of choice. Innumerable combinations are possible, but we shall suggest only a few of these, in connection with some of the drugs and preparations available.

It should be remembered that coughing serves to remove mucus from the respiratory tract and often requires no treatment. If, however, the cough becomes unduly severe, it may require alleviation; if the secretion is scanty it may be increased or rendered more liquid.

Acute bronchitis may be divided into two general stages, with certain expectorants useful in each stage, but this is not to be taken as a rigid classification.

The first stage—that of dryness of the mucous membrane, with considerable cough—calls for sedatives; the second—that of free secretion—may require stimulant expectorants.[1]

The prevalence of coughs and "colds" in the winter months is sufficient evidence of the importance of this class of agents. Their use in domestic practice—largely as "patent medicines," so-called—probably exceeds that directed by the physician as ten to one.

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1. The terms "stimulating" and "sedative" used in connection with expectorants refer only to the effect on the centers.

Physicians are supplied liberally with literature by manufacturers of proprietary remedies of this type, but the pharmacology of this literature is not always worthy of the faith that some physicians place in it. As an example we quote from a circular distributed exclusively to physicians: "In severe and frequent cough, when little mucus is secreted, as shown by the scanty viscal sputum, *morphin,* or, better, its derivative, *ethyl-morphin,* is indicated, which *increases secretion* and lowers excitability of the respiratory center." For comparison with this interested statement by the manufacturers we quote (merely for the sake of comparison) from an article on opium in Wood's Therapeutics (11th ed., 716): "Its tendency to check secretion forbids its use, however, in a very large proportion of cases, notably in those in which there is persistent dryness of the bronchial mucous membrane." Sollmann, Cushny and others state that morphin possesses the same property, though to a lesser degree than opium, which is very generally recognized.

The manufacturer of each cough mixture advocates the use of his particular remedy for all coughs, but we may be pardoned if we again quote Wood for comparison: "It is plain that the medical practitioner must study in each individual case the relations between the cough and the amount of work required."

The discovery of a medicinal agent is the signal for a host of imitators whose product may differ, if at all, merely in the substitution of an ethyl for a methyl group, or of one harmless acid radical for another. These are presented in increasing num-

bers to the physician, who can by no possibility remember them all. Or, some well-known drug, whose length of service, if not merit, entitles it to some respect, is seized on to serve as a basis for fabulous claims, perhaps long since voiced, disproved and forgotten.

There is still another interesting phase connected with these various nostrums. Many of us pride ourselves on the fact that we use only "ethical" preparations and also that we insist on knowing just what we are prescribing or using. It must be rather embarrassing, therefore, to find that even the public is more exacting in this respect than we are and that the manufacturers of popular medicines, when they do advertise the composition of their particular mixture, publish a full and complete formula and not an incomplete one such as we frequently find in the advertising pages of medical journals, or in the circulars that come to our desks.

SEDATIVE EXPECTORANTS.

Among the official sedative expectorants to be used in the first, or dry, stage of cough, we have ipecac, tartar emetic, apomorphin, senega and other nauseants.

Ipecac contains two alkaloids, emetin and cephælin, of which emetin is the more abundant and much the more active, and upon which the action of the crude drug mainly depends.

Ipecac is extremely irritant to mucous surfaces, causing conjunctivitis and irritation of the nasal passages, with active secretion when brought into contact with those tissues, and nausea and vomiting when it is taken into the stomach. If a suffi-

cient amount of the drug escapes evacuation during emesis and passes into the intestine the irritation causes increased peristalsis, diarrhea, and even bloody stools.

It is generally accepted as a fact that ipecac causes vomiting by its direct action on the stomach, and not by acting on the center, as apomorphin does.

As in the case of other nauseants, ipecac causes increased secretion by the salivary glands and by the mucous glands of the respiratory tract. This effect is more lasting with ipecac than with apomorphin and certain other emetics; hence its greater value in expectorant mixtures. Furthermore, it causes much less depression than tartar emetic, and this is a decided advantage in many cases.

Emetin is not well suited for subcutaneous injection, as it is extremely irritant.

The mode of action of ipecac in tropical dysentery is unknown.

Tartar emetic, like ipecac, acts directly on the stomach to cause emesis. This conclusion is not materially affected by the oft-quoted fact that emesis may be induced in an animal by this drug after the stomach has been replaced by the bladder of a pig.

Most of the drug is evacuated during the vomiting which it causes, but if a sufficient amount escapes into the intestine it gives rise to symptoms closely resembling those caused by arsenic, and it is stated that as small a dose as two grains has proved fatal.

The nausea is accompanied by the usual effects on the pulse and mucous and salivary secretion.

Emesis usually follows an effective dose within twenty minutes, but, owing to the great depression which this drug produces, it is not nearly so useful as an emetic as apomorphin, ipecac or one of the other metallic emetics, such as copper sulphate, but the nauseant dose is only about one-fifth that necessary for emesis; hence it does not cause sufficient depression to interfere with its use in the case of robust patients.

Apomorphin induces vomiting by direct action on the medulla, acting much more promptly and in smaller doses after subcutaneous injection than when given by the mouth. Small doses cause nausea, with the usual attendant symptoms, increased pulse rate and increased secretion of mucus and saliva. The nausea is usually of but brief duration, but it is sometimes very persistent. Therapeutic doses of apomorphin have very little narcotic action and no perceptible effect on the heart.

IPECACUANHA.—U. S. P.—Ipecac is the dried root of *Cephaelis Ipecacuanha* (Brotero), A. Richard (Fam. *Rubiaceæ*). It is known commercially as Rio, Brazilian or Para ipecac, or the corresponding portion of *C. acuminata,* Karsten, known commercially as Carthagena ipecac, yielding, when assayed by the process given in the Pharmacopeia, not less than 2 per cent. of ipecac alkaloids. Ipecacuanha was first described by Piso and Markgraf, in 1648, in their natural history of Brazil. The drug appears to have been well known to the na-

tives of Brazil and to have been much prized for a variety of therapeutic purposes. It was introduced into Europe, about 1675, by John Helvetius, of Paris. The Carthagena variety of ipecacuanha is a comparatively recent introduction, being first noted as a distinct variety, about 1870. Ipecacuanha is official in all pharmacopeias, but up to the present time the Pharmacopeia of the United States is the only one to recognize the Carthagena variety as being the equal of the Brazilian.

PULVIS IPECACUANHÆ.—U. S. P.—Average dose: Expectorant, 0.050 gm. (1 grain); emetic, 1 gm. (15 grains).

FLUIDEXTRACTUM IPECACUANHÆ.—U. S. P. —Fluidextract of Ipecac.—This should contain 1.75 per cent. of alkaloids.

Average dose: Emetic, 1 c.c. (15 minims); expectorant, 0.05 c.c. (1 minim).

PULVIS IPECACUANHÆ ET OPII.—U. S. P.—Powder of Ipecac and Opium (Dover's powder). This contains 10 per cent. of ipecac, 10 per cent. of powdered opium and 80 per cent. of sugar of milk.

Average dose: 0.500 gm. (7½ grains); used chiefly as a diaphoretic.

SYRUPUS IPECACUANHÆ.—U. S. P.—Syrup of Ipecac. This contains 7 per cent. of fluidextract of ipecac and 1 per cent. of acetic acid in a mixture of glycerin, sugar and water.

Average dose: Expectorant, 1 c.c. (15 minims); emetic, 15 c.c. (4 fluidrams).

VINUM IPECACUANHÆ.—U. S. P.—Wine of Ipecac. A mixture of 10 per cent. of fluidextract of

ipecac, 10 per cent. of alcohol, and 80 per cent. of white wine.

Average dose: 1 c.c. (15 minims).

SENEGA.—U. S. P.—Root of *Polygala senega.*—This is one of the few drugs of American origin that has found a place in every recent pharmacopeia. It contains a saponin which is locally irritant, but which is not absorbed; hence, the drug is not depressing. It is almost invariably used in small amount as an addition to other expectorants. It has the disadvantage of an unpleasant acrid taste. The official preparations are:

FLUIDEXTRACTUM SENEGÆ.—U. S. P.—Average dose, 1 c.c. (15 minims), and

SYRUPUS SENEGÆ.—U. S. P.—This contains 20 c.c. fluidextract of senega in 100 c.c.

Average dose: 4 c.c. (1 fluidram).

See also compound syrup of squill.

Another irritant nauseant more notable for its abuse than its use is:

SANGUINARIA.—U. S. P.—Rhizome of *Sanguinaria canadensis* (bloodroot). This drug, usually omitted by modern therapeutists or dismissed with a line, contains sanguinarin, belonging to the morphin group, and causing depression of the respiratory center. It is mentioned here more particularly because of its widespread use by the nostrum makers. The common name—bloodroot—appears to possess considerable psychical effect. The only official preparation is:

FLUIDEXTRACTUM SANGUINARIÆ.—U. S. P.

Average dose: 0.1 c.c. (1½ minims).

The "Compound Syrup of White Pine" of the National Formulary represents the "popular" expectorant. It is not recommended, however, as it is too complex.[2]

ANTIMONII ET POTASSII TARTRAS.—U. S. P.—Antimony and Potassium Tartrate; tartar-emetic. Colorless, transparent crystals or a white, granular powder, soluble in 15.5 parts of water. This is the most popular and widely used of the medicinal compounds of antimony, and is now official in all recent pharmacopeias.

Average dose: Expectorant, 0.005 gm. (1/10 grain); emetic, 0.03 gm. (½ grain).

VINUM ANTIMONII.—U. S. P.—Wine of Antimony. This contains 0.4 per cent. of antimony and potassium tartrate dissolved in a mixture of 1 part of alcohol and 5 parts of white wine, and enters into the well-known compound mixture of glycyrrhiza—a deservedly popular expectorant.

Average dose: Of the wine 1 c.c. (15 minims).

Tartar emetic is also an ingredient (0.2 per cent.) in the compound syrup of squill.

APOMORPHINÆ HYDROCHLORIDUM.—U. S. P.—Apomorphin Hydrochlorid.—The hydrochlorid of an alkaloid prepared from morphin by the abstrac-

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2. The following is the formula for the Compound Syrup of White Pine:

White pine bark (pinus strobus)	℥iiss	75
Wild cherry bark	℥iiss	75
Spikenard root	ʒiiss	10
Balm of Gilead buds	ʒiiss	10
Sanguinaria root	ʒii	8
Sassafras bark	grs. cv	7
Morphin sulphate	grs. viiss	0
Chloroform	ʒiss	6
Sugar	℥xxvss	750
Alcohol		
Water		
Syrup (U. S. P.), of each to make	Oii	1000

tion of one molecule of water. It is soluble in 40 parts of water, in the same proportion of alcohol, practically insoluble in all other solvents.

Apomorphin is much less useful as an expectorant than as an emetic, its action being brief.

Average dose: Expectorant, 0.002 gm. (2 mg. or 1/30 grain); emetic, 0.005 gm. (5 mg. or 1/12 grain).

IPECAC.

When the bronchi are inflamed and the secretion is scanty or thick and tenacious, nauseants, such as ipecac, lead to increased secretion which secures its removal by coughing. The choice of nauseants is guided by the general condition of the patient, ipecac being preferred to antimony and potassium tartrate in those cases (children and weakly persons) in which great depression would be dangerous. The active principle of ipecac is not usually employed in the pure state as an expectorant, the syrup of ipecac being preferred, as the tannin present retards absorption and prolongs the action.

The expectorant dose of nauseants is always very much less than the emetic—approximately one-tenth or less in the case of ipecac. The average doses given are approximate and the expectorant dose is to be repeated every two or three hours; the emetic dose is to be repeated half-hourly until effective.

For croup in small children few remedies enjoy a greater reputation than syrup of ipecac, which is given alone in doses of from ten to thirty drops, repeated at intervals of thirty minutes until vomiting occurs.

The preparations of ipecac are seldom used alone as expectorants, but are usually added to mixtures of allied use.

The following may be considered a typical prescription for ipecac to be used in teaspoonful doses every two hours; for the syrup of ipecac a corresponding amount of fluidextract or wine may be substituted. When an opiate is imperatively demanded 15 c.c. (4 drams) of comphorated tincture of opium may be added without other change:

℞. Syrupi ipecacuanhæ .....f℥vi 25
Ammonii chloridi .....ʒiss 6
Syrupi tolutani, q. s. ad.....f℥iii 100
Sig.: A teaspoonful at a dose.

ANTIMONY.

Antimony and potassium tartrate is a more depressing nauseant than ipecac and senega. It may be used on robust persons, but not with safety on children or the infirm. Its mode of action is similar to that of ipecac, and here, too, we have a variety of official preparations.

For the administration of antimony and potassium tartrate, the official compound mixture of glycyrrhiza (6 per cent. wine of antimony, 0.024 per cent. antimony and potassium tartrate) is used alone or with ammonium chlorid as follows:

℞. Ammonii chlor. .....ʒi 4
Mist. glycyrrhizæ comp., q. s. ad.f℥iii 100
Misce.
Sig.: Shake the bottle and take a teaspoonful.

Another very popular form of expectorant into which tartar emetic enters is the compound syrup of squill, combining the stimulation of squill and the nauseant action of the tartar emetic. It may

be given alone or with ammonium chlorid as follows:

℞.	Syrupi scillæ comp.	f℥iss	50
	Ammonii chloridi	ʒii	8
	Aquæ, q. s. ad	f℥iii	100

Misce.

Sig.: A teaspoonful every three hours.

STIMULATING EXPECTORANTS.

The stimulating expectorants include a number of balsamic resins (of which benzoic or cinnamic acid is a constituent), creosote, terebene, ammonium carbonate and to a less extent the chlorid.

The preparations of tolu are to be regarded more as vehicles than as actively stimulating expectorants.

Squill is used as an expectorant mainly for its nauseant effect.

Terebene and terpin hydrate are excreted by the lungs and exert a mild stimulation and antisepsis, but the latter properly must be insignificant.

While ammonium carbonate is distinctly stimulating, therapeutic doses of the chlorid have but little action on the centers. Both of these salts assist in the liquefaction of mucus.

BALSAMUM TOLUTANUM.—U. S. P.—Balsam of Tolu is a balsam obtained from *Toluifera balsamum,* and occurs as a yellowish-brown plastic solid that has a pleasant aromatic odor and a mild aromatic taste. It is readily soluble in alcohol, nearly insoluble in water. Balsam of tolu was first described by Monardes, a Spanish physician, about 1574. The drug, it is said, was collected in a district called Tolu, near Carthagena, and appears to have been well known to, and used

by, the natives of Northern South America. Balsam of tolu is widely used at the present time and is official in all the leading pharmacopeias.

Average dose: 1 gm. (15 grains).

SYRUPUS TOLUTANUS.—U. S. P.—Syrup of Tolu, containing the water-soluble principles of 5 per cent. of tincture of tolu in syrup.

Average dose: 15 c.c. (4 fluidrams).

TINCTURA TOLUTANA.—U. S. P.—Tincture of Tolu, a 20 per cent. solution of tolu in alcohol.

Average dose: 2 c.c. (30 minims).

The mildest of the stimulant expectorants is syrup of tolu, if, indeed, this can be considered as anything more than a flavored syrup. The balsam is not frequently used in medicine, but may be given in the form of an emulsion made with acacia and water and sweetened with sugar.

The benzoic acid and volatile oil in the balsam give it the advantage of being mildly antiseptic, the syrup, however, being too weak to be effective in the dose usually employed.

BALSAMUM PERUVIANUM.—U. S. P.—Balsam of Peru may be used in the same dose and for the same purpose as balsam of tolu.

Attention is called to the fact that the urine of persons taking such amounts of these balsams gives a precipitate with nitric acid which may be mistaken for albumin, but the precipitated resins dissolve in alcohol, while albumin does not.

BENZOINUM.—U. S. P.—This balsamic resin is also a harmless stimulant, useful in bronchial irritation.

TINCTURE BENZOINI.—U. S. P.—A 20 per cent. solution of benzoin in alcohol, or:

TINCTURA BENZOINI COMPOSITA.—U. S. P.—"Turlington's balsam," commonly called "Friar's balsam" (containing benzoin, aloes, storax and tolu), may also be given.

Average dose: 1 c.c. (15 minims) every two hours.

The fact that these expectorants are harmless is a very great advantage—and is a point to be particularly remembered in the treatment of small children, in whom opiates and such depressants as antimony and potassium tartrate are to be avoided.

SCILLA.—U. S. P.—Squill. The bulb of *Urginea maritima,* containing several potent principles; it is exceedingly irritant and in large doses toxic.

Average dose: 0.1 gm. (2 grains).

Of all official drugs used in the treatment of cough, few are better known than squill, the syrup being the most popular of its preparations.

This drug is both stimulant and nauseant; hence, it is used in both stages of bronchitis.

SYRUPUS SCILLÆ.—U. S. P.—Syrup of Squill. This represents 5 per cent. of squill; made from vinegar of squill, and, therefore, containing dilute acetic acid; it is, of course, incompatible with ammonium carbonate—a fact not infrequently lost sight of by the prescriber.

Average dose: 2 c.c. (30 minims).

ACETUM SCILLÆ.—U. S. P.—Vinegar of Squill. This represents 10 per cent. of the drug extracted with dilute acetic acid.

Average dose: 1 c.c. (15 minims).

FLUIDEXTRACTUM SCILLÆ.—U. S. P.

Average dose: 0.1 c.c. (2 minims).

TINCTURA SCILLÆ.—U. S. P.—This represents 10 per cent. of the drug.

Average dose: 1 c.c. (15 minims).

These last three preparations of squill are seldom employed, but the following is widely used:

SYRUPUS SCILLÆ COMPOSITUS.—U. S. P.—Compound Syrup of Squill (Hive Syrup). This represents 8 per cent. of the fluidextracts of squill and senega and 0.2 per cent. of antimony and potassium tartrate or about 0.01 gm. (1/6 grain) to the teaspoonful.

Average dose: 2 c.c. (30 minims).

SYRUPUS PICIS LIQUIDÆ.—U. S. P.—Syrup of Tar.—Containing one-half of 1 per cent. of the soluble principles of tar in syrup, is mildly stimulant and the taste is not unpleasant.

Average dose: 4 c.c. (1 fluidram).

Tar itself has a disagreeable acid taste and is not often used in substance.

TERPINI HYDRAS.—U. S. P.—Terpin Hydrate.—This is a substance closely related to turpentine, camphor, etc. It occurs in colorless, lustrous, rhombic prisms, or a white crystalline powder, nearly colorless, of a slightly aromatic and somewhat bitter taste, soluble in about 200 parts of water and in 10 parts of alcohol.

Average dose: 0.1 gm. (2 grains) in capsules or elixir.

Terpin hydrate has been known for some time, but was not used in medicine until after Lepine published the results of his physiologic investigation in 1885. It is supposed to possess the antiseptic and stimulating effects of turpentine without possessing its irritating properties. The sub-

stance soon became popular and was included in the United States Pharmacopeia for 1890. It is official in the German Pharmacopeia and in the French Codex.

TEREBENUM.—U. S. P.—Terebene.—This is a polymerization product derived from turpentine, which it closely resembles.

It is a colorless liquid, having a rather agreeable odor and an aromatic, somewhat terebinthinate taste, readily soluble in 3 times its volume of alcohol, but only slightly soluble in water.

First obtained by Soubeiran and Capitaine about 1841, it was introduced into medicine by Dr. William Murrell about 1885; it was made official in 1890 and in the British Pharmacopeia of 1898.

Average dose: 0.5 c.c. (8 minims).

CREOSOTUM.—U. S. P.—(or Guaiacol.—U. S. P., which constitutes up to 90 per cent. of creosote).

Average dose: 0.2 c.c. (3 minims).

AMMONII CHLORIDUM.—U. S. P.—A white crystalline powder, without odor, having a cooling saline taste, permanent in air, soluble in 2 parts of water and in 50 parts of alcohol.

As sal ammoniac, this substance has been known from a very early time. It is popularly supposed to have been first obtained from the neighborhood of the Temple of Jupiter Ammon, in Northern Africa.

Average dose: 0.5 gm. (8 grains).

Ammonium chlorid was known to the Arabian physicians and was described by Geber. It is now official in all pharmacopeias. Wood recommends this salt in the stage just before secretion

becomes free; for this purpose the following may be used:

TROCHISCI AMMONII CHLORIDI.—U. S. P.—Each troche contains 0.1 gm. (1½ grains) ammonium chlorid and 0.2 gm. (3 grains) extract of glycyrrhiza.

Ammonium chlorid is much used as an addition to compound mixture of glycyrrhiza in the proportion of 4 gm. (60 grains) to 60 c.c. (2 ounces), and it may be added to nearly any expectorant mixture which is not strongly alcoholic.

AMMONII CARBONAS.—U. S. P.—Ammonium Carbonate. This consists of white, hard, translucent, striated masses of a strong odor of ammonia without empyreuma, and a sharp, saline taste, slowly but completely soluble in about 4 parts of water and decomposed by hot water.

Squill in the form of the simple syrup is recommended for use in the latter stages of bronchitis. The compound syrup, containing antimony, is not generally suited for young children, but it has been used in spasmodic croup.

The use of squill as an emetic is not free from danger and the drug is seldom so employed alone.

The following is suggested as a form of prescribing the syrup:

℞.	Syrupi scillæ	f℥i	30
	Syrupi ipecac	f℥i	4
	Ammonii chlor.	℥i	4
	Syrupi tolut., q. s.	f℥iii	100

M. et Sig.: A teaspoonful as required.

When the inflammation affects the upper part of the respiratory passages it is treated with antiseptics, demulcents and anodynes. The lozenges of ammonium chlorid will be found very useful

for this condition. Ammonium chlorid is very commonly used with the compound mixture of glycyrrhiza, but it is not well suited for combination with terpin hydrate, since the latter requires a strongly alcoholic menstruum which precipitates ammonium chlorid.

Terpin hydrate has been suggested as a remedy in a variety of ailments, but it appears to be useful mainly as an expectorant, enjoying a reputation particularly among the nostrum venders. It is in reality useful in aiding to get rid of secretion from the bronchial mucous membrane.

It may be prescribed as the unofficial Elixir of Terpin Hydrate and Codein Sulphate. Dose: Two teaspoonfuls, containing 0.12 gm. (2 grains) terpin hydrate and 0.015 gm. (¼ grain) codein.

Owing to its slight solubility in water, the elixir must be strongly alcoholic—a serious objection to its general use. It is very commonly associated with codein, which is not to be recommended for routine practice.

Terebene is used in much the same conditions as terpin hydrate, but its immiscibility with the mixtures usually employed as expectorants has interfered in no small way with its employment. It may be prescribed in alcoholic solution, in capsules or in the form of an emulsion as follows:

℞.	Terebeni	ʒvi	25
	Pulv. acaciæ	ʒiv	15
	Syrupi tolut.	f℥i	30
	Aquæ, q. s. ad	℥iii	100

M. Ft. emulsum.
Sig.: A teaspoonful as required.

Creosote is used as a stimulant expectorant. There is considerable diversity of opinion as to its

mode of action. It seems to possess little germicidal action so far as the lungs are concerned. When it is administered in a bland oil very large doses are tolerated, but these are not necessary for its expectorant effect.

Numerous compounds of creosote and of guaiacol have been suggested as substitutes for the official products, but it is not probable that they possess any decided advantages over the official. Those which are less poisonous are probably absorbed from the alimentary canal to a much less degree than are the official creosote and guaiacol.

Among the guaiacol compounds is the proprietary "Ethacol," containing ethyl-morphin, a fact to be carefully borne in mind, as the name of the preparation is not nearly so suggestive of morphin as of guaiacol. The manufacturers of this article recommended morphin or ethyl-morphin in bronchitis for *increasing* secretion!

A condition deserving especial mention is that in which the mucus is particularly thick and tenacious, requiring liquefaction; for this purpose, ammonium carbonate is frequently added to other expectorants; it has the disadvantage of an unpleasant taste, which can not be disguised with diluted acids because these decompose the carbonates.

The cough of chronic bronchitis requires the use of one of the stimulant expectorants, such as terebene or terpin hydrate, bearing in mind the avoidance of those which will prove objectionable with continued use.

While urging the advantage of using the pharmacopeial expectorants, we particularly suggest

that the physician consider the several ingredients of any nostrum instead of accepting the absurd, and often grotesque, claims of the manufacturer.

ANODYNES.

When the irritability of the throat causes excessive coughing, anodynes are indicated.

The pharmacology of morphin, codein and some of the morphin derivatives will be discussed briefly in the succeeding chapter, but we wish to reiterate the oft-repeated warning concerning the indiscriminate use of the drugs of this class which do unquestionably relieve coughing, thus giving the patient the impression that he is being cured, whereas the inflammatory process may be progressing. The derivatives of morphin, such as codein and heroin, lessen the irritability of the center without causing so much gastrointestinal disturbance as morphin. Morphin is particularly to be avoided when the cough is attended with free secretion, since the cough is necessary in that event.

CODEINA.—U. S. P.—Codein. Very soluble in alcohol, much less soluble in water.

CODEINÆ PHOSPHAS.—U. S. P.

CODEINÆ SULPHAS.—U. S. P.—Both are quite soluble in water, but not in alcohol.

Average dose: 0.03 gm. (30 mg. or ½ grain).

ACIDUM HYDROCYANICUM DILUTUM.—U. S. P.—Contains 2 per cent. absolute HCN.

Average dose: 0.1 c.c. (1½ minims).

SYRUPUS PRUNI VIRGINIANÆ.—U. S. P.—Syrup of Wild Cherry represents 15 per cent. of bark and 15 per cent. of glycerin.

Codein undoubtedly lessens cough, but, as already stated, this is not always desirable. Codein phosphate or sulphate, being soluble in water, may be added to almost any cough mixture which is not alkaline.

The following is suggested as a simple prescription containing codein:

℞.	Codeinæ sulph.	gr. viii	5
	Ammonii chloridi	ʒiss	6
	Syrupi pruni virg., q. s. ad	f℥iii	100

M. Sig.: A teaspoonful every two or three hours.

Compound mixture of glycyrrhiza, syrup of tar, syrup of squill or syrup of tolu may be substituted wholly or in part, for the syrup of wild cherry.

Codein, rather than its salts, is suited for combination with terpin hydrate, since both require alcohol as solvent.

Codein has come very largely into use in expectorant mixtures in recent years, partly because its action resembles that of morphin without disturbing digestion or causing constipation in moderate doses, partly, no doubt, because manufacturers have popularized it in order to avoid the stigma attaching to the general use of morphin and opium.

Numerous substitutes have been introduced for morphin and codein, but it has not been demonstrated that they possess all the advantages and none of the disadvantages of the officials. It must not be forgotten that the habit may be formed with any of the morphin derivatives, including codein.

The bromids of ammonium, potassium and sodium are safer than morphin, and are frequently beneficial when anodynes are indicated. Their

doses should, however, be more than proportionately reduced for children.

Hydrocyanic acid may be added to expectorant mixtures, but its action is fleeting and it must be frequently repeated.

DEMULCENT EXPECTORANTS.

Demulcents are frequently employed to allay the irritation of the mucous membrane, and they possess the great advantage of being harmless. They may be administered in the form of lozenges or troches.

The following demulcents may be used as vehicles:

SYRUPUS ACACIÆ.—U. S. P.

MUCILAGO ACACIÆ.—U. S. P.

GLYCYRRHIZA.—U. S. P.—Licorice Root is so well known as to require but little comment. Its preparations afford a variety of forms for administering it.

FLUIDEXTRACTUM GLYCYRRHIZÆ.—U. S. P.—This is the Fluidextract of Licorice Root, from which a satisfactory syrup may be prepared by mixing 25 c.c. of the fluidextract with enough syrup to make 100 c.c.

Average dose: 2 c.c. (30 minims).

EXTRACTUM GLYCYRRHIZÆ PURUM.—U. S. P.—This is a semi-solid extract prepared from the root and is well adapted as an addition to extemporaneous mixtures.

Average dose: 1 gm. (15 grains).

TROCHISCI GLYCYRRHIZÆ ET OPII.—U. S. P.—These contain 0.005 gm. (5 mg. or 1/12 grain) of opium.

GLYCYRRHIZINUM AMMONIATUM.—U. S. P.—Ammoniated Glycyrrhizin is an excellent demulcent; it is readily soluble in water, but incompatible with acids.

Average dose: about 0.25 gm. (4 grains).

PULVIS GLYCYRRHIZÆ COMPOSITUS.—U. S. P.—Compound Powder of Glycyrrhiza, a laxative, containing senna, washed sulphur, glycyrrhiza, sugar and oil of fennel, and popularly believed to be a desirable adjuvant to expectorant medicines.

Average dose: 4 gm. (60 grains).

MISTURA GLYCYRRHIZÆ COMPOSITA.—U. S. P.—Compound Mixture of Glycyrrhiza, brown mixture, containing purified extract of glycyrrhiza and acacia, each 3 per cent., syrup 5 per cent., with camphorated tincture of opium 12 per cent., wine of antimony 6 per cent. and spirit of nitrous ether 3 per cent.

Average dose: 8 c.c. (2 fluidrams).

This is a deservedly popular expectorant. It is very often prescribed alone, but is also much used as a vehicle for other expectorants, particularly ammonium chlorid.

The demulcents are useful when they may be applied directly to the seat of the inflammation, but they are of less service when the lower passages are affected.

The Mistura Ammonii Chloridi, N. F., affords an example of the use of a demulcent as a vehicle. It consists of 2½ per cent., each, of ammonium chlorid and purified extract of glycyrrhiza with water. The average dose is two teaspoonfuls.

CHAPTER XIII.

ANALGESICS AND SOPORIFICS.

Analgesics and soporifics are among the most important articles in the materia medica, and at the same time, owing to their abuse, among the most harmful.

Pain, accompanied by sleeplessness, occurs in a great variety of conditions, often with an intensity or persistency that imperatively demands alleviation. When such a condition requires medicines for a long time there is danger that the patient will learn the name of the remedy employed and continue its use after the actual necessity for it has passed. Certainly no other class of remedies requires more painstaking care on the part of the physician, not only in the choice of the particular agent to be used, but also in the regulation of the dose.

The only way to secure the best results in the treatment of such conditions is by acquiring an intimate knowledge of the various remedies in this class and by learning how to use them singly or in combination as may be required.

In a given case a combination of hydrated chloral and potassium bromid may be necessary, while in another the latter alone may suffice. The more dangerous hydrated chloral should never be used

when the less harmful bromid will serve the purpose.[1]

If we find that scarcely any two successive patients demand exactly the same prescription of but two ingredients, how very much less is the probability of finding any considerable number each requiring a "shotgun" prescription of five or six substances of widely different action, agreeing only in the one property of producing unconsciousness.

It should be obvious that the conscientious use of analgesics and soporifics demands the thoughtful selection of the remedy with the careful computation of the dose according to the necessities of the individual case—a condition manifestly impossible when one relies on complex, ready-made mixtures, with doses and indications suggested by an interested layman—the manufacturer. The greater the number of individuals who acquire

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1. Should the physician desire to use a compound mixture of hydrated chloral and potassium bromid of the bromidia type he may have the "Mistura Chloralis et Potassii Bromidi Composita" of the National Formulary compounded, as follows:

℞. Chlorali hydrati		
Potassii bromidi, āā.....ʒi-gr. xv	5	
Ext. cannab. ind.		
Ext. hyoscyami, āā.....gr. ⅝		04
Aquæ q. s. ad.....ʒvi	25	

The hydrated chloral and the potassium bromid are dissolved in a little water and the extracts are then dissolved in the solution of the salts mixed with some powdered pumice stone, and the mixture filtered.

Each teaspoonful will contain approximately 1 gm. (15 grains) each of hydrated chloral and potassium bromid; 0.008 gm. (⅛ gr.) each of extract of Indian cannabis and extract of hyoscyamus.

The mixture should be used with caution, and it will usually be found advantageous to omit the extract of Indian cannabis.

This mixture is unscientific in the extreme and we do not commend its use.

such harmful habits the greater are the profits of the nostrum maker.

It is well known that the habitual use of opium, hydrated chloral, the bromids and other narcotics is widespread, but there are few who appreciate the full extent of these practices, or in how far physicians are responsible because of the careless use of these agents, either in simple form or as an ingredient of some nostrum.

For convenient consideration we shall divide these remedies into opium, atropin, acetanilid, hydrated chloral and bromid groups, the first three being more properly analgesics and the last two soporifics, though no absolute distinction can be drawn between them.

MORPHIN.

The importance of opium and morphin are such that their actions and uses should be carefully studied in standard works of the day, and we shall pass to the minor members of the group after discussing the official preparations briefly.

Morphin constitutes about one-eighth of the weight of opium, the therapeutic properties of which it represents fully; hence we shall consider the pharmacology of the alkaloid briefly.

The action of morphin on the central nervous system has been compared to the "law of dissolution," the higher centers being affected first, reason and judgment are impaired, the sensitiveness to constant pain is diminished, and the patient becomes drowsy, falls asleep or sinks into a comatose condition dependent on the dose. It is a curious fact that, despite the lessened sensibility to a

constant stimulus, such as pain, there may be, after moderate doses, a hypersensitiveness to bright flashes of light and sharp noises.

The widespread use of opium and morphin for local action—injections and lotions—is based on an erroneous idea. Opium contains gum which is a demulcent, a rather expensive one, however, while its active principle, morphin, must be absorbed before it can produce its effects, which are constitutional, not local.

The excitement caused by morphin, in some patients, is explained by the fact that reason and judgment, which under normal conditions impose restraint, are in abeyance, and not by any stimulation by the drug.

The cat reacts to morphin by an extraordinary degree of excitement and the theory of the abeyance of self-imposed restraint as suggested in man is not a satisfactory explanation of this excitement in the cat.

Stimulation of the cord sometimes follows the use of morphin in children, and, after large doses, in the frog this gives rise to strychnin-like convulsions.

Small doses of morphin depress the respiratory center, causing a much slower and somewhat deeper respiration, but the volume of respiration is markedly diminished. The depression of this center explains the use, and also the contraindications of opiates in cough.

Morphin exerts very little influence, in moderate doses, on the other medullary centers, so that the heart and blood pressure are not materially affected, except indirectly as the result of nausea,

when that occurs, but there is a dilation of the cutaneous vessels of certain regions, particularly of the head and face. The seat of this action is not determined with certainty, but it probably explains the diaphoretic action of opium.

The secretion of mucus is usually diminished, except in the case of nausea. The urine is not affected appreciably, but the bladder may become distended owing to the loss of reflex from the sphincter.

Small doses of morphin lessen peristalsis, while an enormous dose given to a dog results in vomiting and diarrhea. These actions are not fully understood, but it seems probable that the action is partly central, though mainly local. The effect of the reflex mechanism in the intestinal wall diminishing peristalsis in the one case and irritation of the intestine during excretion causing the diarrhea. Against this latter and in favor of the participation by the center is the rapidity of action after subcutaneous injection.

The toxicology of morphin is important because of the frequency with which it is taken with suicidal intent. The tincture of opium perhaps is the preparation most frequently used for that purpose, and when this is swallowed the odor may, usually, be detected in the breath.

Morphin is excreted from the blood into the stomach and intestine; hence the stomach should be washed out in all cases of opium and morphin poisoning, regardless of the method of administration, and particularly when the case is seen early. When the stomach has been emptied of food, a very dilute solution of potassium perman-

ganate should be added to the water used in washing that organ.

Death, in cases of morphin poisoning, results from failure of respiration, and, after evacuating the stomach, measures of relief are directed to sustaining the respiratory center. Caffein, by hypodermic injection, or, better, by very strong hot tea, made quickly, not by long standing on the leaves, or strong hot coffee, stimulates the respiratory center directly, also indirectly and more beneficially, by increasing the blood pressure and, therefore, the circulation in the respiratory center. The head may be lowered if the patient is asleep. Violent measures, such as enforced motion and painful slapping, stimulate the respiratory center, but they also increase the work and help to exhaust it, and should not be used.

Strychnin injected subcutaneously, but no more than the therapeutic dose, should be given, but this must not be repeated. Warm, not hot, tea or coffee may be absorbed from the intestine when the pation can not be aroused.

Unlike most alkaloids, morphin is not excreted in the urine; hence diuretics are useless for hastening elimination.

Codein is methyl-morphin. Morphin appears to have the formula:

$$C_{14}H_{10}(OH)_2 \begin{cases} N(CH_3)CH_2 \\ OCH_2 \end{cases}$$

and codein has a similar formula, except that an OCH_3 group replaces one of the CH groups.

Dionin is ethyl-morphin and heroin is di-

acetyl-morphin; in the latter case both CH groups have been replaced.

Cushny states that most impartial observers have failed to obtain better results from heroin and dionin than from morphin and codein in coughs, and that further investigation is required before they can be recommended as being superior to the older and better known alkaloids.

The action of codein resembles that of morphin in a general way, but it is much weaker. It has less of the narcotic and more of the stimulating action on the cord. The respiratory center is not depressed to the same extent and there is less interference with peristalsis.

The danger that the patient will form the truly terrible opium habit from even a short use of the drug or of any of its derivatives should always be borne in mind, and when it is necessary to use them they should be masked. Hypodermics in pain have come to be almost synonymous with morphin in the minds of the laity. This idea should be uprooted both by the use of the method for many other substances and by avoiding it as much as possible with morphin. The odor and the taste of opium and of the tincture, unfortunately, are well known and they should be disguised if possible.

To disguise the identity of opium and its preparations it is customary with some practitioners to employ the old designation thebaica for opium, tincture thebaica for the tincture. The use of the deodorized preparations of opium is also to be recommended for this purpose.

The official titles coming under the heading opium are numerous and important. Opium and granulated opium are never used directly in the practice of medicine, but powdered opium and deodorized opium are frequently prescribed.

OPII PULVIS.—U. S. P.—When assayed, by the process given in the Pharmacopeia, this should yield not less than 12 per cent. nor more than 12.5 per cent. of crystallized morphin. This requirement is somewhat higher than the provision adopted for the International Standard, which limits the morphin contents of powdered opium to 10 per cent.

Average dose: U. S. P. powdered opium is 0.050 (50 mg. or 1 grain).

OPIUM DEODORATUM.[2]—U. S. P.—This is powdered opium which has been treated with purified petroleum benzin to remove the caoutchouc, wax, oil and the odorous substances that are present; the alkaloidal strength and the dose of deodorized opium are the same as for the official powdered opium.

EXTRACTUM OPII.—U. S. P.—Assayed to contain 20 per cent. of morphin. This preparation is now little used, except in suppositories and the official opium plaster.

Average dose: 0.30 gm. (30 mg. or ½ grain).

PILULÆ OPII.—U. S. P.—These are each composed of opium, 0.065 (1 grain), and soap 0.020

2. This preparation is superior to the widely used proprietary preparation of opium "Svapnia," over which it has the advantage of economy, activity and even general reliability, since the accompanying directions for assay are not alone accurate, but are readily followed by any one versed in chemical assay work.

(1/3 grain). These pills constitute a very ancient form of administering opium.

There are five liquid preparations, the least useful of which will be mentioned first:

VINUM OPII.—U. S. P.—Containing 10 per cent. of opium in fortified white wine, aromatized with 1 per cent., each, of cinnamon and cloves. It resembles the well-known "Laudanum of Sydenham."

Average dose: 0.5 c.c. (8 minims).

ACETUM OPII.—U. S. P.—Vinegar of Opium, formerly known as black drop, Lancaster drops or Quaker drops, has long been known and extensively used. It contains 10 per cent. of opium and 3 per cent. of nutmeg in diluted acetic acid, sweetened with sugar.

Average dose: 0.5 c.c. (8 minims).

TINCTURA OPII.—U. S. P.—Tincture of Opium is the well-known and widely used laudanum, and consists of 10 per cent. of opium in diluted alcohol.

Average dose: 0.5 c.c. (8 minims).

TINCTURA OPII CAMPHORATA.—U. S. P.—This, also known as paregoric or paregoric elixir, is the most widely used of the compound preparations of opium now official. It is so well known as a mild anodyne and sedative that further notice is not necessary.

Average dose: 8 c.c. (2 fluidrams). This amount contains about 0.03 gm. (½ grain), each, of powdered opium, benzoic acid, camphor and oil of anise.

TINCTURA OPII DEODORATI.—U. S. P.—Deodorized Tincture of Opium is practically a 10 per

cent. aqueous extract of opium that has been treated with purified petroleum benzin to remove the odorous and other objectionable constituents, and subsequently preserved by the addition of 20 per cent. of alcohol. This, like the simple tincture of opium, is directed to yield, on assay, not less than 1.2 per cent. nor more than 1.25 per cent. of morphin in crystals. The average dose is 0.5 c.c. (8 minims).

While there has been some controversy concerning the origin of this particular preparation, there has never been any difference of opinion as to its potency for harm. From the sedative elixirs of nearly a century ago to the Scotch oats essence of the present day there have been many attempts to exploit deodorized or masked opium preparations, as harmless vegetable compounds. Another class of preparations, like "McMunn's Elixir of Opium," has been exploited as embodying some wonderful discovery in the treatment of opium.[3] The official deodorized tincture is in every way distinctly superior to all of these nostrums, because, as noted under deodorized opium, it has the advantage of economy, efficiency and reliability.

There are but three other galenical preparations of opium official in the present Pharmacopeia.

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3. "Papine" would be a gem among these if the claims made for it were true, but we can not believe that any preparation of opium containing the pain relieving principle (which we know to be morphin) can be "a safe opiate for children under one year." This affords a good example of the audacity of the nostrum vendor who seeks to delude the physician and induce him to foster such vicious habits even in the cradle.

TINCTURA IPECACUANHÆ ET OPII.—U. S. P.—Liquid Dover's powder. This is of practically the same strength as the well-known powder of ipecac and opium.

Average dose: 0.5 c.c. (8 minims).

PULVIS IPECACUANHÆ ET OPII.—U. S. P.—This has been noticed under ipecac (see Chapter IX). It contains 10 per cent., each, of ipecac and of powdered opium.

Average dose: 0.500 gm. (7½ grains).

TROCHISCI GLYCYRRHIZÆ ET OPII.—U. S. P.—These have been previously noticed.

The alkaloids, morphin and codein, are of nearly as much interest as opium.

Morphin was discovered by Sertürner, a German apothecary, in 1805, and was used in medicine as early as 1820. There are four official preparations:

MORPHINA.—U. S. P.—This alkaloid, obtained from opium, occurs as colorless or white shining rhombic prisms or as fine needles or as a crystalline powder. It is odorless and has a bitter taste.

Average dose: 0.010 gm. (1/5 grain).

MORPHINÆ ACETAS.—U. S. P.—This salt of morphin should be kept in well-stoppered, dark amber-colored bottles, and a minute quantity of free acetic acid should be present to prevent decomposition.

Average dose: 0.015 gm. (¼ grain).

MORPHINÆ HYDROCHLORIDUM.—U. S. P.—Like the acetate, this should be kept in well-stoppered dark bottles.

Average dose: 0.015 gm. (¼ grain).

MORPHINÆ SULPHAS.—U. S. P.—Like the other morphin salts, this should be kept in well-stoppered dark bottles.

Average dose: 0.015 gm. (¼ grain).

Sulphate of morphin is much the most frequently used in this country, while the hydrochlorid is generally given the preference in Europe. The acetate is the most readily soluble in water, but is quite unstable, losing acetic acid on exposure to the air, and, as the alkaloid morphin requires 3,300 parts of water for solution at ordinary temperatures, considerable care should be exercised in the use of old, and possibly decomposed, samples of morphin acetate.

While the new Pharmacopeia gives 0.015 gm. (¼ grain) as the average dose of the salts of morphin, we believe that this is too high as the "average" dose.

Codein and two of its salts are official:

CODEINA.—U. S. P.

CODIENÆ PHOSPHAS.—U. S. P.

CODEINÆ SULPHAS.—U. S. P.

Average dose (of either): 0.03 gm. (½ grain).

Codein, in addition to being obtained from opium, is also prepared from morphin by methylation. It was discovered by a French chemist, E. Robiquet, in 1832, but was not generally used in the practice of medicine until many years later. It was admitted into the U. S. Pharmacopeia in 1880; the phosphate and the sulphate are now official for the first time. The sulphate is the form most frequently employed in this country, though it appears to be but little known abroad, where the phosphate is mainly used. The phosphate was

considered under "Expectorants." Codein has been considered a somewhat uncertain drug, owing to its frequent contamination with morphin, but the Pharmacopeia provides a test for its purity, and particularly for detecting the presence of the more poisonous alkaloid.

The phosphate being readily soluble in 2.5 parts of water, is particularly well suited for hypodermic use; or it may be prescribed alone in syrup or combined with hydrated chloral or the bromids; in the latter case the mixture should be directed to be shaken before using.

The average dose of codein or of any of its salts is 0.03 gm. (30 mg. or ½ grain).

APOMORPHINÆ HYDROCHLORIDUM.—U. S. P.—which was also mentioned under "Expectorants," has been recently brought to notice as a hypnotic, in doses of 0.002 gm. (1/30 grain). It is said to have the great advantage of not producing a drug habit.

Heroin and dionin are proprietary names for articles of the morphin group possessing some advantages, but they are not free from danger. The heroin habit is beginning to be common and should be carefully guarded against.

CANNABIS INDICA.—U. S. P.—Indian Cannabis is a well-known member of the opium group. It occurs in dark-green or brownish compressed masses, having an agreeable narcotic odor and characteristic taste.

It appears to have been used by the Hindoos from very early time. It was also known to the Egyptians and to Dioscorides, but it was not introduced into England until about 1835.

Average dose: 0.05 gm. (1 grain), but rarely used in substance.

EXTRACTUM CANNABIS INDICÆ.—U. S. P.

Average dose: 0.01 gm. (10 mg. 1/5 grain).

FLUIDEXTRACTUM CANNABIS INDICÆ.—U. S. P.

Average dose: 0.05 c.c. (1 minim).

TINCTURA CANNABIS INDICÆ.—U. S. P.—represents 10 per cent. of the drug extracted with alcohol.

Average dose: 0.5 c.c. (10 minims).

At one time Indian Cannabis was supposed to have great virtues as an antispasmodic, analgesic and narcotic, and it was highly recommended by a few physicians as a vasomotor stimulant, uterine stimulant, etc. It is now but little used and there seem to be few conditions in which one of the preparations of opium could not be used advantageously in its stead.[4]

Two other members of the opium group are sanguinaria, which we have had occasion to mention elsewhere, and the feebly-acting

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4. It may be worth while to notice the importance attached to the extract of cannabis indica by the makers of bromidia, who claim that their preparation is the only hypnotic that has stood the test in every country for thirty years. Since all the other constituents are very commonly used, one must infer that they consider the genuine imported extract of cannabis indica of exceptional value. Bromidia, it is claimed by the manufacturer, contains 15 grains each of hydrated chloral and potassium bromid, and ⅛ grain each of genuine imported extract of cannabis indica and extract of hyoscyamus, to the teaspoonful. Thus a single repetition of the dose—one teaspoonful—might prove fatal, since 30 grains of hydrated chloral have caused death; but the manufacturers advise *hourly* doses so long as may be necessary to induce sleep. The extravagant claims made by the manufacturers of this nostrum have induced many physicians to use it in preference to prescribing the several official constituents according to individual needs, and to-day it is offered direct to the public at cut-rate prices.

LACTUCARIUM.—U. S. P.

Average dose: 1 gm. (15 grains).

TINCTURA LACTUCARII.—U. S. P.—This is a 50 per cent. preparation of lactucarium made with diluted alcohol.

Average dose: 2 c.c. (30 minims).

SYRUPUS LACTUCARII.—U. S. P.—This is much more commonly employed than the tincture, its popularity being largely due to a nostrum.

Average dose: 8 c.c. (2 fluidrams).

The indications for opium and morphin are too varied for anything like a comprehensive treatment here. This is well illustrated by the remark of Sydenham, who said that few would be callous enough to practice therapeutics without opium. We should always remember, however, that no drug is more frequently misused or lends itself so readily to abuse as opium and its derivatives.

Pain calls for opium. Bearing in mind its numerous disadvantages and possibilities for harm, this is the principal guide to its employment. Cough, at certain stages, diarrhea, severe colic, especially lead colic, inaccessible hemorrhage and conditions calling for a diaphoretic (with ipecac), are among the numerous indications for its use.

For sleeplessness, in the absence of pain, morphin is not nearly so useful as chloral and the bromids. The danger of even very small doses of morphin and opium for children must be borne in mind constantly, and parents should be thoroughly warned of the dangers of soothing syrups. A single drop of tincture of opium is said to have proved fatal to a child under 1 year of age.

THE ATROPIN GROUP.

The atropin group includes the crude drugs yielding the mydriatic alkaloids, such as atropin, hyoscyamin and hyoscin, or scopolamin, all of the latter being closely related chemically.

The actions of atropin and its congeners are so important and so complex that it is entirely beyond the scope of the present article to attempt anything like a complete description of them. The reader can not avail himself of this potent and important class of agents without a careful study of their pharmacologic and therapeutic actions. We shall, therefore, call attention to a few of the more important applications and contraindications without entering deeply into the reasons.

Atropin is not nearly so important as an analgesic as morphin, but it has a variety of uses, several of which will be considered now, while others will be discussed under circulatory stimulants.

Atropin is useful as an analgesic mainly when the pain is of spasmodic origin and when the application may be made directly to the nerve ends of the affected tissues. In the pains of lead colic this may be accomplished by the internal use of one of the preparations of belladonna, preferably a pill of the extract coated with salol or keratin.

Atropin stimulates the central nervous system, being antagonistic to morphin to a considerable degree. The stimulation of the medulla is much the more important in therapeutics.

Atropin paralyzes the terminations of nerves concerned in nearly all the body secretions (mucus, saliva and gastric juice, but not the pancreatic), the vagus endings in the heart (besides those con-

cerned in secretion), and most endings in plain muscle, except those in the vessels.

The influence of atropin on peristalsis is not positively determined, but it seems probable that it only prevents colic pain caused by purgatives without interfering with peristalsis.

Among the results of the action of atropin are: mental excitement, increased respiration (respiratory center), dryness of throat (mucous glands), dilation of the pupil (endings in circular muscle), rapid heart (vagus depression), increased blood pressure (vasomotor stimulation). Atropin depresses sensory endings in the skin when applied locally, but not after internal use.

The most prominent action of atropin is seen in the dilation of the pupil, but the more rapidly acting and less enduring homatropin hydrochlorid is usually preferred for this purpose, if the object is merely to examine the eye—atropin, if it is desired to paralyze accommodation for some time, as in inflammatory conditions.

While the mydriatic effect is so similar with the different members of this group, it must be remembered that they have very dissimilar actions on the brain.

The crude drugs and their preparations belonging to this class are so numerous and so well known that it is hardly necessary to enumerate them. Besides Belladonna Root and Leaves, Hyoscyamus and Stramonium Leaves, a member now official for the first time, is Scopola.

SCOPOLA.—U. S. P.—The dried rhizome of *Scopola carniolica* (Jacquin) (Fam. *Solanaceæ*), yielding, when assayed as directed in the Pharma-

copeia, not less than 0.5 per cent. of its alkaloids, has little odor and a sweetish, afterward bitterish, acrid taste. Though described by Dr. Scopoli in 1771, it attracted but little attention from the medical profession until it was used in manufacturing "belladonna" plasters.

Average dose: 0.04 gm. (2/3 grain).

FLUIDEXTRACTUM SCOPOLÆ.—U. S. P.

Average dose: 0.05 c.c. (1 minim).

SCOPOLAMINÆ HYDROBROMIDUM.—U. S. P.—This is chemically, and otherwise, identical with Hyoscinæ Hydrobromidum, U. S. P. See also Chapter XI.

It has been used in the treatment of nervous excitement, particularly of the insane. It often induces quiet sleep at night—not usually in the day—and may also lessen sexual excitement. Atropin, on the other hand, has been used to stimulate the brain in cases of depression.

Average dose: 0.005 gm. (0.5 mg. or 1/125 grain).

HYOSCYAMINÆ HYDROBROMIDUM, U. S. P., and HYOSCYAMINÆ SULPHAS.—U. S. P.—These are used very much as scopolamin is.

Average dose: 0.005 gm. (0.5 mg. or 1/120 grain).

None of the mydriatic alkaloids should be used as soporifics except in case of urgent need, as the benefits may be more than counterbalanced by the disadvantages. Hyoscin or scopolamin and hyoscyamin are of little use directly in relieving pain; hence, they can hardly be considered as analgesics.

Any of these alkaloids may be given alone as

tablet triturates or as compressed tablets, hypodermically or alone in aqueous solution.

The following is a common method of exhibiting belladonna, particularly in asthma:

℞.	Tincturæ belladonnæ fol.	
	Tincturæ lobeliæ, āā.....f℥ii	10
	Spiritus ætheris nitrosi, q. s. ad..f℥iii	100

Of this a teaspoonful is given every hour or two until relief is obtained.

The bromids of ammonium, sodium or potassium may be used with the prescription given, but in that case adjuvant or aromatic elixir should be substituted for the spirit of nitrous ether, and, as in every case when bromids or iodids are combined with alkaloids, the mixture is directed to be shaken.

The extracts of the crude drugs are much to be preferred to the alkaloids as additions to purgatives, since the latter would be largely absorbed from the stomach, whereas the local action on the intestine is desired.

THE ACETANILID GROUP.

Phenacetin, antipyrin and acetanilid reduce the febrile temperature through their action on the heat-regulating center. This reduction is due to increased heat loss mainly, for the lessened production of heat *follows* the change. The increased loss of heat is accomplished by the dilation of the cutaneous vessels, rather than by sweating, for it occurs when sweating is prevented by the use of atropin. The dilation is of central origin and does not affect the splanchnic area, the blood pressure being affected but little.

Therapeutic doses of the antipyretics increase the heart rate somewhat at first, but this is unim-

portant, and when the fever abates from any cause the pulse and the respiration become slower and stronger.

Very large doses induce sleep, then convulsions, cyanosis and collapse.

Small doses relieve headache and neuralgia, but their mode of action is unknown.

Acetanilid is rapidly, phenacetin slowly, oxidized in the body with the formation of para-amido-phenol or a closely related substance, which acts on the hemoglobin of the blood, forming methemoglobin, and to this the cyanosis caused by these drugs is usually attributed, but this does not seem to be a wholly satisfactory explanation in every case. Since phenacetin is decomposed more slowly than acetanilid, it is not so active, but it is safer and the action is more prolonged. Antipyrin is not decomposed in the body, but is excreted in the urine unchanged.

It is decidedly preferable for the practitioner to study the action of one or two of these agents while accurately observing the effects on his patients, rather than experiment with a large number of them.

While large doses of these antipyretics are usually borne very well, it should be remembered that many people present a peculiar idiosyncrasy and even ordinary doses may cause cyanosis and alarming collapse, while the heart becomes extremely weak and even death may result, particularly in febrile patients. Even the same patient may react quite differently at different times toward the same antipyretic.

The official salicylic acid, discovered in 1839,

was introduced as an antiseptic in 1873 and later as an antipyretic. The salicylates now find their greatest usefulness in the treatment of acute rheumatism. They have been discussed in connection with internal antiseptics.

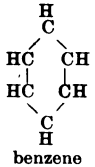
CHEMISTRY OF THESE PREPARATIONS.

A brief review of the chemistry of the antipyretic group will show the relationship of the various members to each other.

Quinin being a derivative of quinolin, many attempts were made to produce it synthetically, with the resulting discovery of a number of quinolin derivatives which possess antipyretic properties, but all of them dangerous because of their tendency to produce collapse. All of these are now practically obsolete.

Another substance having antipyretic action is phenylhydrazin, which is of interest because of its derivative, antipyrin. Hydrazin, N_2H_4 (or $H_2N{-}NH_2$), which is formed by the union of hydroxylamin and ammonia, usually exists in combination with an organic radical.

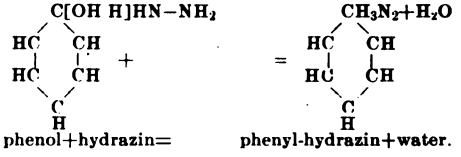
Starting with the benzene ring C_5H_6,



benzene

phenol (carbolic acid) is formed by replacing an H with OH. If this OH in turn be displaced by

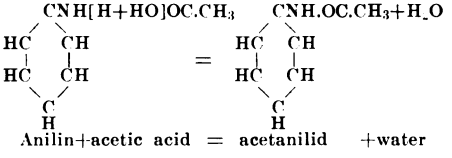
the hydrazin radical, phenyl hydrazin is formed thus:



Though many derivatives of phenyl-hydrazin have been exploited, antipyrin and its compounds are the only ones in general use.

When the practitioner uses drugs which at best are so potent for harm he will do well to employ them in their simplest form rather than in such unofficial combinations as hypnal (chloral and antipyrin) or salipyrin (salicylic acid and antipyrin).

Acetanilid or phenyl-acet-amid is obtained by the action of boiling glacial acetic acid on anilin. By introducing "acet" before "amid" the chemic name is derived.

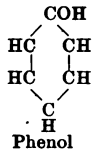


When other acid radicals replace that of acetic acid similar compounds are formed, which are in no wise superior to the official. Thus we have benzanilid and exalgin (or methyl acetanilid), the latter differing from acetanilid only in having a CH_3 group replacing an H.

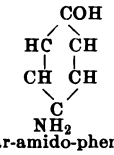
It will be understood from its chemistry why acetanilid can be prepared so cheaply and, there-

fore, why it is so extensively employed in the nostrum traffic.

Phenetidin is important as the basis of the phenacetin group. Chemically it is the ethyl ester (sulphuric, so called) of amido-phenol. We have par-amido-phenol, and if the OH is then replaced by the ethyl radical we have phenetidin.



Phenol



Par-amido-phenol

Various acid radicals may replace an H of the NH_2. If it be the acetic radical we have phenacetin, if lactic acid we have lactophenin.

These formulas may appear complex, but a careful examination of them will show the relationship existing between the various members of the group. If the practitioner finds the official phenacetin unsuited to his purpose in a given case, it is not probable that another compound, differing merely in the nature of an acid radical, will prove more beneficial.

Among the phenetidin series there are, besides the official phenacetin, many in which the syllable "phen" indicates the phenetidin source. They include phenocoll, salophen, lactophenin and many others.

We shall have occasion to mention urethane (ethyl carbamate) among the hydrated chloral group, and it may be said that several of its derivatives have been used as antipyretics, but they do not merit further consideration here.

In connection with the subject of antipyretics we may mention a number of substances which, except historically, are now of little interest. Kairin, discovered by Dr. O. Fisher in 1882, was the first of the coal-tar compounds to be introduced as an antipyretic on the strength of physiologic experiments. It was also one of the first of the medicinal synthetic chemicals to be patented. The older physicians may remember its widespread use and some of the exaggerated claims that were made for it and how, despite this, it fell into disfavor and was soon forgotten.

Thallin, made by Dr. Skraup in 1884 and investigated in the clinic of Nothnagel, soon shared the fate of kairin, despite liberal advertising.

The enormous growth of the traffic in proprietary remedies mainly composed of acetanilid and allied substances was probably the most potent factor in arousing physicians to a realization of the part they play—often unconsciously—in furthering the selfish schemes of unprincipled manufacturers. The Council on Pharmacy and Chemistry of the American Medical Association has shown that antikamnia, phenalgin, salacetin and ammonol were mere mixtures of acetanilid with other substances, and the federal pure food and drugs law has demonstrated that some of them, at least, have been changed in composition and now contain phenacetin.

We can, therefore, no longer prescribe these mixtures under the impression that we are using true chemical compounds. It is probable that acetanilid figures more extensively in self-drugging than does any other single substance.

The following are official:

ACETANILIDUM.—U. S. P.—Acetanilid, antifebrin or phenylacetamid, the monacetyl derivative of anilin, occurs in colorless crystalline laminæ or powder, permanent in air, odorless, of a slightly burning taste, and very slightly soluble in water.

It was first prepared by Gerhard in 1852, but was not used medicinally until nearly thirty years later, when it was introduced under the trademark name of antifebrin. It is now employed very extensively, its extreme cheapness—less than 2 cents an ounce—causing it to be used as the basis of many pretended synthetics.

Average dose: 0.20 gm. (3 grains).

PULVIS ACETANILIDI COMPOSITUS.—U. S. P. – This has been made official to serve as a substitute of uniform standard for the host of more or less similar compounds, such as we have enumerated above, which have come into such unfortunate vogue.

The official preparation consists of 70 per cent. of acetanilid, 10 per cent. of caffein and 20 per cent. of sodium bicarbonate.

Average dose: 0.3 gm. (5 grains).[5]

ACETPHENETIDINUM.—U. S. P.—Acetphenetidin, better known as phenacetin, is official in the

5. It should be noticed that the dose of acetanilid in the mixture is larger than the official dose of acetanilid; yet it is supposed to act more effectively when mixed with sodium bicarbonate. It is to be regretted that such a combination has been given official recognition. The reason, of course, is evident—persistent advertising of certain nostrums has created an abnormal demand for acetanilid combined with a supposed heart stimulant. But, as it is extremely improbable that caffein does counteract the harmful effects of acetanilid, it is not wise to recognize such a combination even to meet a supposed demand.

British, German and other European pharmacopeias as Phenacetinum. It is officially described as Acet-para-phenetidin, a phenol derivative, the product of the acetylization of par-amido-phenetol. Phenacetin occurs as white glistening scales or a fine crystalline powder, odorless and nearly tasteless. It is soluble in 925 parts of water and in 12 parts of alcohol.

Average dose: 0.5 gm. (8 grains).

ANTIPYRINA.—U. S. P.—Antipyrin is official in France as Analgesin, in Great Britain as Phenazonum, and in Germany as Pyrazolonum—phenyl-dimethylicum. Chemically, it is described as phenyl-dimethyl-pyrazolon, and is obtained by the condensation of phenyl-hydrazin with aceto-acetic acid and subsequent methylation of the product. Antipyrin occurs as a colorless, almost odorless, bitter tasting, crystalline powder, that is readily soluble in water and soluble in about 1 part of alcohol.

Average dose: 0.250 gm. (4 grains).

Antipyrin was first prepared by Dr. L. Knorr of Erlangen, in 1884; it was investigated physiologically by Professor Filehne, who reported it as an active antipyretic.

It will be more satisfactory to consider the therapeutics of these antipyretics collectively, with occasional comments on the separate members of the group.

They are mostly used for headache and for the reduction of temperature in fevers of an intermittent type, but it must not be forgotten that they do not remove the underlying cause, and that the

use of these drugs in continued fevers is liable to be harmful, since the temperature is sure to return to its former height, or to go even higher, when the action of the antipyretic has worn off.

The alarming collapse that may follow even a moderate dose of acetanilid serves as a warning against its use when there is reason to suspect any tendency to that condition. On the other hand, a sudden lowering of the temperature in fever may result in collapse symptoms wholly independently of the nature of the remedy employed. Acetanilid has the greatest and phenacetin the least tendency to produce collapse among the official preparations of this nature. It is, in part, to overcome this tendency that caffein is used in the official compound acetanilid powder, but it is doubtful if it is of any great value in guarding against this collapse, though it does appear to enhance the analgesic action of this class of remedies. There can be little doubt that many of the sudden deaths, of which we so constantly read, occurring without apparent cause on the streets and elsewhere, are in reality due to overdosing with nostrums containing acetanilid.

Women should be particularly cautioned against the promiscuous use of nostrums of the compound acetanilid powder type during menstruation.

When it is remembered that antipyrin and acetanilid are derived from phenylhydrazin, and anilin—active blood poisons—it is not surprising that the official derivatives possess the properties of these drugs in a minor degree.

The collapse seen after ingestion of the anti-

pyretics, particularly acetanilid (least with phenacetin), is due to several causes. Probably the most frequent cause is the mere lowering of the temperature which exposes the collapse actually existing but hidden by the high temperature. This result is not to be charged to the antipyretic. It is treated exactly as collapse from any other cause would be—by stimulation. Very large doses of the antipyretics act on the heart muscle, causing depression. and on the vasomotor center, causing collapse.

The acetanilid habit is not rare and it leads to a deplorable condition, but the symptoms generally disappear when the drug is withdrawn.

Profuse perspiration is a disagreeable effect, more frequently seen after acetanilid and antipyrin than after phenacetin. If this is so annoying as to demand interference, a hypodermic injection of 0.5 mg. (1/120 grain) of atropin will be found effective. Redness and irritation of the skin are frequently seen after the use of the various antipyretics of this group. They are probably due to vasomotor changes.

Antipyrin in solution has been used extensively to check the bleeding of superficial wounds, and all the various members of this group are to some extent antiseptic.

While so much space has been devoted to the contraindications and untoward effects of these agents, it is not with a view of discouraging their use, but rather that the physician may avoid the disappointments which arise from their use in unfavorable conditions.

Acetanilid may be given alone in powder or in capsules, in adjuvant or aromatic elixir, or suspended in syrup or mucilage of acacia. The compound acetanilid powder affords a convenient form for the relief of headache. A dose of 0.3 gm. (5 grains) in powder or capsule is usually effective; this may be repeated once in an hour if necessary, but further repetition is to be avoided.

Compressed tablets of such insoluble substances as phenacetin and acetanilid are not recommended as they disintegrate slowly.

An acetanilid powder, containing ammonium carbonate instead of caffein, is used in the German Hospital of Philadelphia,[6] when it is desired to avoid the cerebral stimulation of caffein.

Antipyrin is very soluble in water and in alcohol, and hence it may be given in simple aqueous solution, in aromatic elixir or in powdered form, but not in combination with other active remedies, as it is readily decomposed.

Acetphenetidinum (phenacetin), being less objectionable than acetanilid and antipyrin, may be expected to replace them very largely now that the price is reduced. Its insolubility in water has led to its extensive use in powder and in capsules.

A combination of phenacetin, caffein and sodium

6.

℞.	Acetanilidi	
	Sodii bicarb., āā.....grs. xxii	1|5
	Ammon. carb. .....grs. xi	|75

This is sufficient for ten powders of about 0.3 gm. (5 grains) each, one being given every three or four hours to reduce fever. For headache one is given and repeated, if necessary, in an hour.

bromid has attained considerable popularity; these may be combined in various ways.[7]

The antipyretic action of these drugs is obtained best by administering them when a natural remission of the fever begins.

Acetanilid causes a more prompt fall of the temperature, while the action of phenacetin is more lasting.

Small doses are usually effective in typhoid fever, but even large amounts are often ineffective in pneumonia and septic conditions.

The relative value of the antipyretics of this class and the cold bath is still the subject of dispute, and circumstances must determine which is to be used in any case. In districts where trained attendants are not to be had the careful use of the antipyretics is certainly preferable to the cold bath given by inexperienced nurses, or by indifferent orderlies, as is the custom in some of the large hospitals in New York, for example.

7.

℞.	Acetphenetidini (phenacetin) ...grs. xv	1	5
	Caffeinæ .....grs. viii		
	Sodii bromidi .....ʒi	4	
	Elixir adjuvantis .....f℥iii	100	

The mixture is to be shaken and two teaspoonfuls given as a dose. This is often used for headache, one dose being usually sufficient.

Still another, widely used, mixture containing acetanilid, is a migraine elixir that is being exploited by a number of manufacturers. A representative formula, for a preparation of this kind, may be given as follows:

℞.	Acetanilidi .....gr. xxx	2	2
	Caffeinæ .....gr. iii		
	Sodii bromidi .....ʒii	8	
	Alcoholis .....fʒi	4	
	Elixir aromatici q. s. ft.....f℥iii	100	

Average dose 5 c.c., or 1 teaspoonful.

If 20 c. c. of tincture of cardamom be added to this, or if adjuvant elixir (which is also official) be used instead of the aromatic, the appearance of the mixture will be much enhanced and the psychical effect increased.

THE HYDRATED CHLORAL GROUP.

The hydrated chloral group includes, besides hydrated chloral, chloralformamid (chloralamid), paraldehyd, ethyl carbamate (urethane), sulphonmethane (sulphonal) and sulphonethylmethane (trional). Several of these preparations are so well known that we may dismiss them in a few words, but some of them may be profitably discussed at greater length.

It was formerly supposed that hydrated chloral was decomposed in the body with the formation of chloroform, on which the action of the drug depended. This is now known to be incorrect, for the drug is excreted in the urine, for the most part, as trichlorethyl glycuronic acid.

Hydrated chloral acts very much like chloroform on the heart and on the central nervous system. Small doses act only on the brain, resulting in a lessened mental activity and a diminished receptivity of impressions, thus inducing sleep. The pulse and respiration become slower as in normal sleep. With larger doses there is a depression of the spinal reflexes and of the respiratory and vasomotor centers, the heart is slowed by direct action, as after chloroform. The cutaneous vessels are markedly dilated, and this may cause fall of temperature and sometimes a skin rash.

Death follows large doses, from paralysis of the heart as with chloroform, and the respiration may be paralyzed at the same time.

The same degenerations are seen after hydrated chloral as after chloroform, and the contraindications for the two drugs are the same, degenera-

tion of the heart and vessels, nephritis, gastritis, and depression of the respiratory center.

Hydrated chloral acts as a rubefacient when applied locally, and this irritant action is manifested in the stomach when taken in concentrated solution. It should, therefore, be given well diluted, and large doses are apt to cause gastric irritation even when this precaution is observed.

The same train of symptoms which characterize chronic alcoholism are seen when hydrated chloral is taken for a prolonged period.

Sulphonal is excreted more slowly than it is absorbed, and cumulation may occur. It is contraindicated in nephritis.

It is easy to drug anyone into unconsciousness, but the members of this group do not possess curative properties and at most they only secure rest and sleep for the patient. Hydrated chloral is not free from danger, and we wish to point out some of the dangers attending its use, either alone or in the nostrums which contain it, or closely related substances.[8]

All authorities agree that it is unjustifiable to use large doses of hydrated chloral, either alone or in combination with other official drugs. When a moderate dose of hydrated chloral fails to induce

8. Attention has been called to Bromidia, which is directed to be given in as much as teaspoonful doses every hour until sleep is produced, pain being mentioned as one of the indications for its use. Since hydrated chloral is not an anesthetic, except in unsafe doses, it is readily seen how dangerous this advice is, particularly when we are dealing with such intense pain as that encountered in appendicitis, even admitting that the preparation contains the other ingredients claimed.

It will be noticed that the dose of hydrated chloral given here is only about 7 grains (0.5 gm.), but combined with sodium bromid is effective and quite safe.

sleep in cases of severe pain, it is very much more rational to give a dose of morphin, or other analgesic, than to repeat the hydrated chloral indefinitely. The hydrated chloral habit is not rare, and if its sale at cut rates in the shape of nostrums with fanciful names is to go on unchecked, we can hardly hope to see any diminution of the baneful practice. When we employ hydrated chloral and sodium, or potassium bromid in simple solution it is with full cognizance of the danger, but because the exigencies of the case demand their use, and we only use them with caution.[9] In a general way the contraindications for hydrated chloral are the same as for chloroform. In the present addition of the Pharmacopeia it is official as:

CHLORALUM HYDRATUM.—U. S. P.—Hydrated Chloral.

Average dose: 1 gm. (15 grains).

Of the unofficial, more or less closely related drugs, hypnal (antipyrin and hydrated chloral) has been mentioned.

Somnos is a 5 per cent. solution of chloral glycerolate, also known as trichlorethidene propenyl ether. Its action is identical with that of a 5 per cent. solution of hydrated chloral in a similar vehicle; isopral is trichlorisopropyl alcohol; its

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9. A fairly safe and very efficient hypnotic commonly used in Bellevue Hospital in New York affords a convenient form of using sodium bromid with hydrated chloral.

℞.	Chlorali hydrati	grs. xx	1|30
	Sodii bromidi	grs. lxxx	5|30
	Syr. aurantii	f℥iv	16|
	Aquæ q. s. ad	f℥i	30|

M.

Two teaspoonfuls are given at a dose. This may be twice repeated at intervals of an hour if necessary, but more than two doses are rarely required in suitable cases.

The hydrated chloral may be slightly increased in the prescription, in which case the dose should not be repeated more than once.

action is the same as that of hydrated chloral, but isopral is more active and more toxic.

Dormiol is a combination of amylene hydrate and hydrated chloral, and chloralose, a combination of hydrated chloral and glucose, partakes of the action of morphin and is rather expensive. Chloretone, another of the more recent products, is not entirely devoid of danger and is not always so certain in its action as hydrated chloral, while butyl chloral hydrate or croton chloral hydrate, is one of the older compounds that has been found wanting and is now little used. Of the official compounds of this group we have:

CHLORALFORMAMIDUM.—U. S. P.—Chloralformamid. Chloralamid. This has practically the same action as therapeutic doses of hydrated chloral, the latter being formed in the body by decomposition of chloralformamid.

Average dose: 1 gm. (15 grains).

PARALDEHYDUM.—U. S. P.—Paraldehyd, a transparent liquid, is slower in its action than hydrated chloral, but also safer. It has the disadvantage of a persistently disagreeable taste and odor. It is locally irritant and should not be used in irritable conditions of the stomach. It may be prescribed dissolved in 10 parts of water or in aromatic elixir, and is best administered cold, or followed by a cold drink.

Average dose: 2 c.c. (30 minims).

SULPHONMETHANUM.—U. S. P.—Sulphonmethane, sulphonal, diethylsulphonedimethylmethane, and

SULPHONETHYLMETHANUM.—U. S. P.—Sulphonethylmethane, trional, disulphonmethylethyl-

methane, may be considered together, as they differ chemically only in the addition of an ethyl group in the latter.

Average dose (either) : 1 gm. (15 grains).

The therapeutic action of these two preparations is practically identical, and the closely related tetronal might also be included in this statement. Trional is somewhat more soluble than sulphonal. While these substances are safer than hydrated chloral they are not wholly free from danger, as fatal cases of poisoning have been reported and the sulphonal and trional habits, while of more recent origin, bid fair to equal, if not to exceed, the chloral habit in the number of their victims. These agents are usually given in powder, and owing to their slow absorption should be given about two hours before they are expected to act. To insure more speedy action they may be given in solution, for which purpose they can be dissolved, or at least suspended, in a cup of hot milk.

ÆTHYLIS CARBAMAS.—U. S. P.—Ethyl Carbamate, urethane. This is a new official preparation which is claimed to be much safer than hydrated chloral, to which it would be distinctly superior but for the fact that its action is not so certain and because tolerance is soon acquired. It is best given in water, in which it is very soluble. The average dose is 1 gm. (15 grains).

The therapeutic use of this group of agents is indicated by the term soporific, and by what has been said concerning their pharmacology.

THE BROMID GROUP.

The bromids depress the central nervous system —brain, medulla and cord—simultaneously. The

action on the psychic centers results in mental confusion and impaired memory, the action on the medulla and cord in diminished reflexes. This is especially noticeable in the lessened reflex from the throat, and the bromids were used before the introduction of cocain in examination of the larynx. This also explains the lessened sexual desire, and the depression of the motor and sensory cells explains the value of these agents in epilepsy.

Long continued use of the bromids leads to the condition known as bromism, the most prominent symptoms of which are the skin eruptions of different kinds, the fetid breath, coryza, nausea and vomiting.

The mental depression results in a tendency to sleep, but this is not so restful as that following hydrated chloral, and the patient usually experiences some dulness and mental confusion for some time after awakening. Large doses of potassium bromid depress the heart, but this action is mainly due to the potassium ion, and it does not occur after the use of the other alkaline bromids.

Owing to their depression of the cord the bromids are antagonistic to strychnin.

The excretion of the bromids begins very soon after they are taken, but a long time elapses before they are completely eliminated.

Monobromated camphor has no such action as that of the alkaline bromids, because the bromin ion is not dissociated. It belongs to the camphor group, and, having no advantage over camphor, it should be dismissed from the Pharmacopeia.

The bromids are of considerable historic, as well

as of practical, interest. Potassium bromid was introduced by Balard about 1826, who supposed it to have properties analogous to those of potassium iodid. It was not until some time after 1850 that the present, sedative, uses of the bromids were accidentally discovered. During the past four decades the several alkaline bromids have received considerable attention, and several of them are now official in every pharmacopeia.

The abuses that have arisen in connection with substances belonging to this group are largely due to the misrepresentations that are made in connection with the efficiency or the character of the nostrums containing them.

Strontium salts, particularly the bromid, were brought forward some years since, at exorbitant prices, as being infinitely superior to the corresponding compounds of other elements. Experience has shown that, in the main, these claims were unfounded, though many, even now, claim that strontium bromid disturbs the stomach less than the corresponding sodium or potassium salt. Another claim that is frequently made by manufacturers of nostrums like "Peacock's Bromides," is that they use "chemically pure" salts. Exactly what is meant by this claim it is difficult to say, but the Pharmacopeia gives us a number of readily applied tests by which the salts themselves may be tested. The manufacturers of nostrums, on the other hand, not infrequently add the very substances that are considered contaminations.

The official bromids are freely soluble in water, and they are best directed to be dispensed in aqueous solution, with or without the addition

of some one of the aromatic syrups. The available salts are:

AMMONII BROMIDUM.—U. S. P.

CALCII BROMIDUM.—U. S. P.

LITHII BROMIDUM.—U. S. P.

POTASSII BROMIDUM.—U. S. P.

SODII BROMIDUM.—U. S. P.

STRONTII BROMIDUM.—U. S. P.

Average dose (of any one of these): 1 gm. (15 grains).

ACIDUM HYDROBROMICUM DILUTUM.—U. S. P. —Diluted Hydrobromic Acid contains 10 per cent. of absolute hydrobromic acid.

Average dose: 4 c.c. (1 fluidram).

The bromids are useful in the treatment of epilepsy, for, while a cure is very rarely effected, they lessen the frequency of the attacks in a very large proportion of the cases. Potassium bromid is usually preferred, but some use a mixture of the alkaline bromids. No perceptible effect may be seen for some time after the commencement of the treatment, but with persistence the benefits usually follow. In such cases the skin eruptions may prove very annoying; scrupulous cleanliness should be enjoined, and arsenic may prove useful for the acne.

The bromids are very useful in sleeplessness caused by mental worry, but they are ineffective when it is due to pain.

Bromism increases the patient's susceptibility to contagious diseases, such as pneumonia and bronchitis.

Hydrated chloral acts as a soporific in smaller

doses when a bromid is added, and they may be prescribed somewhat as follows:

℞.	Potass. brom.	ʒiss	6
	Aquæ	f℥i	30
	Aquæ menth. pip., q. s. ad	f℥iii	100

Misce. Sig.: A tablespoonful at a dose.

Of course, any of the alkaline bromids may be used in place of the potassium bromid, but the latter is much the most frequently employed and appears to be the most effective.

The N. F. elixirs of the bromids of ammonium, sodium, potassium and of lithium may be used, but they should be diluted with several times as much water. The routine use of alcoholic liquids, such as these elixirs, is not recommended in those cases where the drug in increasing doses is likely to be continued for some time.

As in the case of other salts, the bromids are irritant to the stomach and should be given well diluted with water—never in the form of compressed tablets—and best after eating.

CHAPTER XIV.

CIRCULATORY STIMULANTS.

The subject of circulatory changes is entirely too extensive for anything like a comprehensive treatment in the limited space that can be allotted to it here, but we shall discuss some of the indications for influencing these changes and try to indicate how they may be brought about.

The term "heart tonic" has been so loosely employed that it is better to avoid it altogether, or to use it only with reference to those drugs which, acting directly on the heart, improve the muscular tone.

The heart is but one, and in some respects even a minor, factor in the question of blood pressure, on which the state of the circulation largely depends. Hence, while a "heart tonic" implies an agent which improves the action of the myocardium, the actual changes in the circulation depend not alone on the amount of work done by the central organ, but on the combination of that and the constriction or dilatation of the blood vessels.

Since the relative amounts of blood existing in the veins and arteries, and the amount which passes through a certain area or organ in a given time are dependent on several more or less closely related factors, we may direct our efforts toward influencing one or more of these factors when we wish to increase or diminish the blood supply of

an organ, or when we wish to hasten the transfer of blood from veins to arteries.

An increase in the rate of the heart or strength of the beat, without a compensating change, either in the heart itself or in the blood vessels, will, of course, increase the general circulation, and conversely, a diminished action would lessen the circulation, but so delicately is the complex circulatory mechanism adjusted that such a simple change probably never occurs alone in the intact body, though it may at times predominate over other accompanying changes.

THE MECHANISM OF STIMULATION.

The simplest means of increasing the blood pressure consists in increasing the strength of the individual beats when they are too weak (whereby the heart is more completely and more forcibly emptied), and securing just enough slowing to enable the heart to dilate more fully and to become filled with a larger volume of blood. These two actions insure a larger volume of blood being thrown into the aorta in a given length of time than occurred under previous conditions. An increased volume of blood with increased force must, of course, insure an increased circulation in those areas in which there is no great change in the caliber of the smaller vessels.

A high blood pressure, on the other hand, may be most simply reduced by slowing the heart without increasing its strength, or by acting on the vessels peripherally or through the vasomotor centers, causing dilation.

The accumulation of an undue amount of blood

in the veins is relieved by increasing the efficiency of the heart as mentioned for raising the blood pressure—by slowing and strengthening its beat—for, as we have seen, this improves the drainage from the veins by lengthening the diastole, while the strengthening throws a larger volume of blood into the arteries.

We may arrange the agents affecting circulation into two groups as follows: Those mainly affecting the heart, directly or indirectly; those mainly affecting the vessels, directly or indirectly.

The most important group of circulatory stimulants consists of digitalis and a number of similarly acting substances. While, as is well known, barium chlorid has an action to some extent similar to that of digitalis, nearly all the other members of this group that are of therapeutic importance are somewhat allied chemically; for the most part the active principles of these drugs are glucosids or resins. The exact chemistry of the drugs of this class is still obscure, despite numerous investigations, and it demands but little consideration here; their pharmacologic action, however, serves to explain their therapeutic indications, and may aid in choosing the one best suited to a given condition.

The circulatory conditions demanding stimulation are mainly those in which undue relaxation occurs, and in which an imperfectly acting heart, including such conditions as valvular insufficiency and stenosis, permits the blood to accumulate in the veins. Any increase in the work of the heart must tend to relieve these conditions, particularly if there is at the same time just sufficient slowing

to secure complete distention of the heart with blood during diastole.

An increase in the strength of the contraction more completely squeezes the venous blood out of the heart muscle, which is then supplied with a larger proportion of arterial blood. The increased force of the pulse wave must first be felt more strongly in the coronary artery than elsewhere, since there is less inertia to be overcome in the much shorter column of blood between the aortic valve and the opening into the coronary artery. The longer diastole then permits a more perfect supply to the capillaries in the heart, thus improving the nutrition of the heart to an even greater degree than would correspond to the extra work thrown on the ventricles by their being compelled to contract against an increased arterial pressure.

As we have just said, the slowing of the heart should be just sufficient to enable the heart to become fully distended, for a greatly slowed heart would suffer in lessened nutrition, because, other things being equal, the rate of flow through the coronary circulation varies with the number of the pulsations in a given space of time.

This improved nutrition of the myocardium is the first essential for a sustained increase in the force of the beats, either from a more energetic action of the unaltered heart or after hypertrophy; because, however, such a muscle might be stimulated to unusual activity, exhaustion and paralysis must follow unless nutrition keeps pace with the work performed. Langendorff has shown experimentally that the energy of the heart is enormously influenced by the available blood supply.

A drug might affect one or more phases of the heart beat, or the local and central action may be in part antagonistic and the effect on the blood pressure in the general circulation will in the latter case be dependent on the kinds of influence and the degree to which each is excited.

Slight slowing with increased strength of contraction may improve the nutrition, and it will be readily understood why it is difficult to secure equally perfect nutrition of the heart when it is made to beat more rapidly, since the only factor here which makes for an improved coronary circulation is the more frequent squeezing out of venous blood by the contractions while all other conditions are unfavorable, a greater number of contractions, each throwing out less blood and meaning more energy expended for a given amount of work performed—a more frequent overcoming of the inertia of the blood in the arteries—so that a very rapid heart soon exhausts itself. For these reasons we do not often seek to raise blood pressure or to improve the general circulation by increasing the rate of the heart unless it is extremely slow.

Shock and collapse are conditions that are due to depression of the respiratory, cardiac and vasomotor centers. The depression of the vasomotor center permits the vessels to dilate and the blood gravitates to the vessels of the splanchnic area, which are capable of holding a very large amount. This dilatation is accompanied by a fall of pressure in the general circulation, less blood goes to the centers and to the coronary circulation, the heart beats more feebly and the respiration becomes weaker. This condition obviously calls for

prompt stimulation of the circulation. It is apparent, however, that a stimulation of the heart alone would only result in increased work while its own nutrition would not be correspondingly improved because the pressure in the coronary circulation can not be greatly increased so long as the voluminous vessels of the splanchnic area offer cavernous spaces for the blood which is pumped from the heart.

Stimulation of the constrictor mechanism of the vessels is urgently demanded in collapse, and this is secured in the mildest cases by gravity determining the blood to the head when the head is placed lower than the body. The centers are toned up by the better blood supply, and this increased tone of the vasomotor center causes constriction of the splanchnic vessels, raises the blood pressure and improves the general circulation, which, in turn, further tones up the centers as well as the heart, which is also stimulated by the improved tone of the cardiac center. The respiration is improved at the same time owing to the improved tone of the respiratory center.

Dr. George Crile has devised a pneumatic suit whereby pressure may be applied to the surface of the limbs, thus forcing a large amount of blood into the body and head, and gravity (lowering the head) may be made to assist in driving it to the head—the essential fact being to supply the medulla with blood.

PHYSIOLOGIC SALT SOLUTION.

Heat, mainly supplied by hot water bottles, should be used with any other measures in shock.

The amount of fluid in the vessels may be considerably increased by injecting, under aseptic precautions, into a vein, or even under the skin, normal saline solution, or, as it is better to term it, physiologic salt solution, made by dissolving 9 grams of sodium chlorid in enough water to make one liter (approximately 132 grains of sodium chlorid to 1 quart of water). The solution should be boiled (to render it sterile) and then cooled to about 40° C. (104° F.). As noted above this solution may be used hypodermically or it may be injected directly into a vein. Another, and at times a very satisfactory, method of attaining the same result is to inject slowly one or two liters of this solution into the rectum, whence it is readily absorbed into the circulation.

Drugs which act on the vasomotor centers are indicated in collapse, but the simple means just enumerated serve, as explained, to tone up the centers in mild cases by an improved blood supply, and they are, of course, preferable to mere stimulation by drugs. Then, too, in proportion to the urgency of the case is the difficulty of securing stimulation of the centers. In profound shock the stimulants of the vasomotor centers appear to have no lasting effect, or to increase the trouble. In collapse of a mild character, however, a vaso-constrictor acting more powerfully on the vessels of the splanchnic area causes the general blood pressure to rise, more blood goes to the centers, and they are placed in a better tone, exactly as is the case when gravity sends the blood to the head.

Hot alcoholic drinks are very commonly em-

ployed in collapse and shock; they probably act reflexly from the stomach.

Some clinicians maintain that morphin improves a weakened heart. As a depressed center is less susceptible to shock from reflex influences, morphin may lessen shock or depression due to pain, and the center will then be able to exert a better influence on the heart. It has often been claimed that opium or morphin caused an increased supply of blood to the brain by dilating the vessels of that organ, and this may account for an increased circulation in the cardiac center and hence an improvement in the heart. The depression of the respiratory center by morphin is rather strong evidence against any stimulation of the cardiac center, however. Morphin has no direct action on the heart and its vasomotor effects are variable.

THE DIGITALIS GROUP.

The pharmacologic action of digitalis and that of its available active principles have been more extensively studied than has been done in the case of any other member of the group. The isolated frog's heart, and later the mammalian, has been used to determine the action on that organ apart from the influence through the center. The rate of the isolated mammalian heart is either increased or little affected by digitalis or its principles, but Gottlieb and Magnus found that the strength of the individual contractions is increased by it and that more actual work is done by the isolated heart. In the intact mammal digitalis slows the heart by stimulation of the vagus center, and the strength of the beat is increased by

the action on the myocardium. The vasomotor centers are stimulated at the same time. The direct results of these several actions have been detailed in the introductory paragraphs.

Digitoxin, the most active of the principles that have been isolated from digitalis, has essentially the same action on the circulatory system as the drug itself, but, being insoluble in water, it is slow in producing its effects. Albert Fraenkel has found that about sixty hours elapsed after a single effective dose was injected, hypodermically, into a cat before the typical action was induced.

Digitalin, or "Digitalinum verum," is somewhat more soluble in water and its action was elicited in twenty-four hours after a dose, corresponding in activity to that of digitoxin just mentioned, was injected into a cat, while strophanthin (obtained from strophanthus seeds), which is very soluble in water, produced its effects much more rapidly. The therapeutic action of these three substances is very similar, but Gottlieb and Magnus found that digitoxin is capable of restoring an irregularly beating heart to rhythmic pulsations to an astonishing degree; indeed, they were able to restore isolated and perfused hearts to strong regular beats after they had gone into delirium cordis.

Digitalis and other members of this group have the great disadvantage of causing cumulative effects when used continuously for some time. Digitoxin produces these effects more readily than strophanthin and digitalin. Fraenkel was able to continue the administration of digitalin daily for many weeks at near the toxic dose without cumulative action. No habituation occurred in this

period, however, thus disproving the claims of Heide, based on a much more shorter period of experimentation, that such takes place.

Gastric irritation is the first evidence of a toxic action from a single toxic dose or from cumulative action, and digitalis, or any of its congeners without exception, must be stopped for a time when cumulative effects are seen. When the heart is slowed by any member of the digitalis group the action is very persistent.

Digitoxin causes constriction of the coronary arteries, but this does not occur after strophanthin.

As noted before, there are other drugs and chemicals that possess a somewhat similar action, but it must be evident to all that nothing is to be gained, and that much harm may result from giving heed to unwarranted and exaggerated claims of the nostrum maker who lauds a preparation which ostensibly depends on some little known drug, such, for instance, as the several species of cactus.

By far the most interesting as well as the most important of the official drugs of the group now under consideration is:

DIGITALIS.[1]—U. S. P.—This consists of the dried leaves of *Digitalis purpurea,* collected from

1. From what we know of the chemistry of this particular drug, and from the action of the known isolated proximate principles, it would appear that in this connection it was particularly unfortunate that the committee on revision did not see its way clear to adhere more strictly to the proposed international standards for the formulas of potent medicaments and direct, for the extraction of digitalis, the proposed 70 per cent. alcohol in place of the diluted alcohol of the U. S. Pharmacopeia. The stronger alcohol would have had the advantage of insuring a more ready and more complete solution of the active principles, of answering better as a preservative and of materially reducing the amount of inert extractive now contained in the official tincture.

the second year's growth at the commencement of flowering. This drug is official in all pharmacopeias and is generally considered as being particularly susceptible to chemical change. It should be carefully preserved and should not be kept for more than one year.

Average dose: 0.05 gm. (1 grain).

While the chemistry of digitalis is far from being thoroughly understood, there are a number of proximate principles derived from digitalis that are now being marketed in a commercial way and which have well-defined chemical as well as physiologic properties; several of them are being extensively used in this country as well as abroad. The most potent of these unofficial articles is:

Digitoxin: This, as has been noted before, is soluble in alcohol, but is nearly insoluble in water. The older and in some respects better known French preparations, variously called digitaline crystallisée, or French digitalin, closely resemble digitoxin in physical properties and also in physiologic activity.

Digitalin (Digitalinum verum, Kiliani): This is a white amorphous glucosid that is readily soluble in alcohol, but only slightly soluble in water. While it is less toxic than digitoxin and may be given in much larger doses, it closely resembles that principle in its therapeutic action and uses.

Digitin (Merck): This is also readily soluble in alcohol and only slightly soluble in water. While still available it is now generally thought to be physiologically inactive as a circulatory stimulant.

Digitalein (Schmiedeberg): This is readily soluble in water and is probably a mixture of several proximate principles.

Digitalin "German": This occurs as a yellowish white, amorphous powder that is soluble in both water and alcohol. It is said to consist of a variable mixture of Digitalinum verum (Kiliani), digitalein and digitonin.

The following are official:

EXTRACTUM DIGITALIS.—U. S. P.—This is made from the fluidextract by evaporation.

Average dose: 0.01 gm. (10 mg. or 1/5 grain).

FLUIDEXTRACTUM DIGITALIS.—U. S. P.—Fluidextract of Digitalis is made with diluted alcohol.

Average dose: 0.05 c.c. (1 minim).

INFUSUM DIGITALIS.—U. S. P.—Infusion of Digitalis contains 1.5 per cent. of digitalis, 10 per cent. of alcohol and 15 per cent. of cinnamon water.

Average dose: 8 c.c. (2 fluidrams).

TINCTURA DIGITALIS.—U. S. P.—This now represents 10 per cent. of the crude drug in diluted alcohol in place of 15 per cent. as formerly official.

Average dose: 1 c.c. (15 minims).

STROPHANTHINUM.—U. S. P.—This is a glucosid, or mixture of glucosids, obtained from strophanthus.

Average dose: 0.003 gm. (0.3 mg. or 1/200 grain).

STROPHANTHUS.—U. S. P.—This consists of the ripe seeds of *Strophanthus Kombé*. It is pref-

erably administered in the form of the official tincture.

TINCTURA STROPHANTHI.—U. S. P.—This preparation now represents 10 per cent. of the drug in 65 per cent. alcohol, and is double the strength of the tincture official in the U. S. Pharmacopeia, 1890.

Average dose: 0.5 c.c. (8 minims).

APOCYNUM.—U. S. P.—This is the dried rhizome of *Apocynum cannabinum,* or of other closely allied species of *Apocynum.* This drug is said to have been used by the American Indians in various ailments, and has long been in use as a household remedy. More recently it has again attracted attention by its possible uses as a circulatory stimulant, though the practical results that have been attained so far do not appear to warrant its use in all cases. The only official preparation is:

FLUIDEXTRACTUM APOCYNI.—U. S. P.—The Fluidextract of Apocynum is directed to be made with a mixture of 10 per cent. of glycerin, 60 per cent. of alcohol and 30 per cent. of water.

Average dose: 1 c.c. (15 minims).

CONVALLARIA.—U. S. P.—This consists of the dried rhizome and roots of *Convallaria majalis.*

Average dose: 0.5 gm. (7½ grains).

FLUIDEXTRACTUM CONVALLARIÆ.—U. S. P.—This is made with a mixture of 65 parts of alcohol and 35 parts of water.

Average dose: 0.5 c.c. (8 minims).

THERAPEUTIC ACTIONS OF THE DIGITALIS GROUP.

Digitalis will be referred to again under the heading of diuretics (Chapter XVI).

As a circulatory stimulant one of the drugs of the digitalis group is indicated when the heart is weak and rapid and the blood pressure low, conditions which arise under a variety of circumstances.

In cardiac dilatation with weak systole digitalis affords our best remedy, as may be readily understood from the pharmacologic action. In pneumonia the right ventricle suffers primarily and digitalis is indicated, for, while it affects the right ventricle less than the left, and the auricle least, this does not affect its usefulness in this condition, because the nutrition of the heart—both left and right—is supported by the improved coronary circulation, a most important factor, as we have seen, when extra work is thrown on the heart, and the pulmonary circulation is not affected directly by the general vasoconstrictor action of the digitalis. In this connection, the lengthened diastole, while it undoubtedly affords a better chance for the emptying of the pulmonary veins, is a factor of but minor importance. The use of digitalis in mitral insufficiency is familiar to all and the pharmacologic action readily explains its usefulness in this connection.

Digitalis and its congeners are said to be harmful in some cases of mitral stenosis, and they may fail to prove beneficial in insufficiency of the aortic valves. It is suggested that in this condition the blood may gravitate from the brain through the aortic valve during the lengthened diastole. This action of the drugs also must be observed carefully in these conditions and they must be withdrawn if they appear to be doing harm.

Drugs of the digitalis series are contraindicated in cases of fatty degeneration of the heart, since a heart so weakened could scarcely support the additional burden imposed by the increased arterial tension, and hypertrophy can not be expected to occur in such a heart. They are also contraindicated in all conditions in which an increasing blood pressure would be dangerous, for instance, in aneurism.

With digitoxin particularly, one must constantly watch for the first symptoms of cumulative action, usually gastric disturbance, and it, or other members of the same group, should be temporarily withdrawn when suggestive symptoms occur.

The tincture of digitalis contains a larger proportion of the alcohol-soluble digitoxin than does the infusion, in which the digitoxin present is held in solution by means of digitonin. Digitoxin being the most irritant of the known principles of digitalis, the infusion, containing digitalin principally, will often be preferred.

When the heart is weak and irregular, digitoxin is probably the most efficient remedy we possess for restoring it to normal contraction. An alcoholic solution of digitoxin may be used to advantage, provided it be well diluted with water when administered.

The dose of digitoxin as given by the different authors is somewhat variable. Cushny states that 1/12 mg. (1/750 grain) of crystalline digitoxin may be given three times daily. Schmiedeberg recommends 1/5 mg. (1/330 grain) of the crystalline digitoxin three times daily, and this has

been supported by clinical experience. The physician will do well not to exceed this latter dose too greatly, bearing in mind that cumulative effects sometimes develop quite suddenly, even with a dose which has been apparently harmless.

Digitoxin and digitalin, pure or in the leaf, are changed into substances with a convulsive action in the presence of moisture, by bacteriologic action, hence old infusions should not be used nor should those leaves be employed which bear evidences of not having been properly dried and carefully preserved.

When Cloetta announced the discovery of a soluble amorphous form of digitoxin, which he named Digalen, it was generally accepted because of Cloetta's standing in the scientific world, but it appears that this preparation has no advantages over other preparations of digitalis, that it is not an aqueous preparation, that its subcutaneous use is painful and finally that it differs but little from a hydroalcoholic solution of ordinary digitoxin.

It is to be hoped that in the next revision of the Pharmacopeia digitalis leaves will be directed to be physiologically assayed, dried with proper care and sealed with the date of assay, for the leaf so prepared has proved more satisfactory in the hands of many clinicians than any of the isolated principles or the Galenical preparations of the drug.

Digitoxin and digitalin may be kept dissolved in alcohol and diluted as required. The dose of digitalin, or digitalinum verum, is from 2 to 6 mg. (1/30 to 1/10 grain) three times daily.

Digitoxin may be prescribed as follows:

℞. Digitoxini (cryst.) .....gr. 1/12 |005
Alcohol, q. s. ad.....f℥iii 100|
M. Ft. solutio.
Sig.: One teaspoonful in a little water three times a day.

Digitalin can be prescribed in the same way, but 0.05 is used in place of 0.005 gm. thus:

℞. Digitalini veri .....gr. i |05
Alcohol, q. s. ad.....f℥iii 100|
M. Ft. solutio.
Sig.: One teaspoonful in water three times daily.

The tincture of digitalis, diluted with water, is given alone three times a day. Owing to the slow excretion it is not necessary to repeat the dose more frequently, and the drug should be stopped for two days about once a week to avoid cumulative effects, whether one of the active principles or a Galenic preparation of digitalis is being used.

Sollmann has suggested that strophanthin may deserve an even greater popularity than digitalis, and this suggestion has found support in more recent investigations. Strophanthin is now official whereas the active principles of digitalis have not as yet been included in our Pharmacopeia.

Strophanthin causes but little vasoconstriction and it, therefore, deserves the preference over digitalis and its principles when increased blood pressure is to be avoided. Thus, when dilatation of the heart is due to high blood pressure from increased arterial tension, strophanthin may be used, or, if digitalis is employed, a vasodilator such as nitroglycerin or one of the nitrites should be given at the same time.

Because of its more prompt effect on the heart,

strophanthin may be employed to usher in the action when digitalis is to be employed. This promptness of action would also render it preferable to digitalis in shock or collapse were it not that the vasoconstrictor action is wanting.

Digitalis, or one of its principles, may be given several hours before an operation when there is reason to apprehend shock, so that its action may coincide with the time that shock occurs instead of waiting till that condition has actually developed before giving the slowly acting remedy.

Strophanthus seed and the tincture were formerly of very variable quality, but at the present time they are fairly uniform.

Strophanthin, the active principle of strophanthus seed, is of constant composition, is very soluble in water and may, therefore, be dispensed in simple solution. However, it undergoes decomposition, in aqueous solutions, and it is, therefore, better to prescribe it in diluted alcohol: 0.01 gm. (1/5 grain) may be directed to be dissolved in 100 c.c. (3 fluidounces) of diluted alcohol and one teaspoonful of this solution, diluted with water, may be given three times a day.

The official strophanthin must not be confused with crystallized strophanthin, g-strophanthin, gratus strophanthin or strophanthin Thoms, as it is variously termed, which is obtained from the seeds of strophanthus gratus, and which is recommended in doses of 5 milligrams (1/12 grain) or 30 milligrams (½ grain) per day, while as much as 0.075 gm. (1¼ grains) per day have been given to an adult. Gratus strophanthin is said to be identical with ouabain, but that, on the

other hand, has been said to be much more toxic, to the frog's heart at least, than ordinary strophanthin. The dose of strophanthin gratus mentioned above is only for internal use, as the glucosid is much more toxic when used subcutaneously.

We may call attention to the fact that the dose of strophanthin given in the Pharmacopeia—1/3 mg. (1/200 grain)—is smaller than that contained in the ordinary dose of the tincture, 0.5 c.c. (8 minims), of which certainly represents more than half a milligram (1/125 grain) of strophanthin, and it has been suggested that the latter has been advised in wholly inadequate doses. It is extremely toxic, however, and the dose must be increased only with great caution.

Dr. H. C. Wood, Jr., recommends Canadian hemp as a satisfactory and reliable circulatory stimulant, but as his published work appears to have been done with a fluidextract of *Apocynum cannabinum* and as the Pharmacopeia itself recognizes closely allied species of apocynum, that may or may not have similar physiologic properties and therapeutic uses, it may be well to await the results of further investigations before trusting too implicitly in the possible results to be obtained from this drug.

Other official members of this group have little to recommend them in preference to the more prominent ones just described.

It might be added that the alkaloid of the suprarenal gland is not suited for long continued administration. It does not influence blood pressure when given by the stomach, and but slightly or not at all when injected just beneath the skin.

When injected into the muscle there is a transient rise of blood pressure. Its local use has been discussed at greater length in connection with astringents (Chapter VIII).

STRYCHNIN.

Strychnin, unlike digitalis, has no perceptible direct action on the heart when therapeutic doses are used, but it produces its circulatory effects wholly by its influence on the centers, except in so far as the local action on the alimentary canal is concerned; this may be disregarded in the present consideration of strychnin, which is commonly injected hypodermically when its circulatory effects are desired.

Therapeutic doses of strychnin cause a rise of blood pressure by stimulation of the vasomotor center; the reflexes are increased, leading to improved tone of the voluntary muscles, and increased muscular activity always tends to increase the heart rate; this tendency, however, is counteracted by the stimulation of the vagus center by strychnin, the heart being slowed or showing little change in frequency. When the slowing is excessive there is a fall of blood pressure despite the vasoconstriction, but this does not usually occur. If the tendency to increased frequency predominates over the vagus stimulation the rise of blood pressure is further augmented.

As strychnin operates readily to produce its effects it is a most valuable remedy when a quick rise of blood pressure is required. So rapidly are its effects elicited that convulsions may occur in a frog within two minutes of the injection of a toxic

dose, and after a massive dose a rabbit may give a single convulsive leap into the air and be apparently lifeless from paralysis of the respiratory and other centers when it strikes the operating table.

Biberfeld has investigated its mode of action on the respiratory center. He depressed the respiration by morphin, after which strychnin was injected: this usually resulted in a greater increase in the volume (sometimes even exceeding that before the administration of morphin) than in the frequency.

The following preparations are official:

STRYCHNINA.[2]—U. S. P.—This is an alkaloid obtained from nux vomica; it is also obtainable from other plants of the *Loganiaceæ*.

Strychnin is only slightly soluble in water, 1 to 6400, but it is soluble in 110 parts of alcohol.

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2. Owing to the frequency with which poisoning by strychnin occurs, its toxicology deserves brief mention here.

As is well known, strychnin causes a characteristic type of convulsion rather closely resembling tetanus. The amount of the alkaloid that is necessary to produce this toxic effect is much greater, however, than is usually supposed; but, on the other hand, when once a large amount has actually entered the circulation, there is little hope of ultimate recovery. As death is due to paralysis of the respiratory center life may be prolonged, and a possible recovery brought about, by carrying on artificial respiration. This, however, should be begun before natural respiration ceases or even before it becomes very greatly depressed.

Strychnin requires several days (3 to 8) for its total elimination. Diuretics hasten elimination and may be of benefit when the amount of the poison that has been taken does not greatly exceed the minimum fatal dose.

Cushny advises strong tea (infusion) when the patient is seen with the strychnin in the stomach. This advice seems to be based on a misconception of the capacity of tea tannin for forming the insoluble tannate.

The fact that strychnin acts directly by paralyzing the respiratory center fully explains the possible danger that may result from the use of a stomach tube, and it will not be necessary to repeat this frequent caution.

STRYCHNINÆ SULPHAS.—U. S. P.—This is the salt of strychnin that is most extensively used in this country; it contains five molecules of water and approximately 78 per cent. of strychnin alkaloid. Strychnin sulphate is soluble in 31 parts of water and in 65 parts of alcohol.

On the continent of Europe the preference is usually accorded to the nitrate. This is official in our Pharmacopeia as:

STRYCHNINÆ NITRAS.—U. S. P.—This represents 84 per cent. of strychnin alkaloid and is soluble in 42 parts of water or in 120 parts of alcohol.

The average dose of either of the official preparations is given as 0.001 gm. (1 mg. or 1/64 gr.).

Strychnin is useful in all forms of low blood pressure because of its action on the vasomotor center.

There can be little doubt of the beneficial effects of strychnin in many cases of shock or collapse, but when irrecoverable shock exists it appears to depress further the centers after an extremely brief stimulation.[3]

To secure its greatest usefulness in conditions of this kind strychnin should be given hypodermically, or to secure an even quicker action it should be injected deeply into the muscle of the arm or thigh. This method of hypodermic injection is

3. Crile defines surgical shock as an exhaustion of the vasomotor centers, the cardiac and respiratory centers being only secondarily involved, and collapse as due to a suspension of the functions of the cardiac or vasomotor centers or to hemorrhage. Of course, an exhausted or paralyzed structure can not be stimulated. Sollmann defines both shock and collapse as a sudden depression of the activity of the medullary center; if of reflex origin, shock; if direct, collapse. We employ the terms in the latter sense. A depressed center may be stimulated.

usually to be preferred, as it is less painful than injections just beneath the skin.

Strychnin is one of the best respiratory stimulants and in an emergency large doses may be given. It is always to be remembered that strychnin is a remedy for the crisis and is not to be used as digitalis is, to maintain blood pressure for a considerable length of time.

When paralysis of the limbs is due to a lesion in the cord which completely blocks the transmission of nerve impulses strychnin can do no good, since it has no peripheral action, but if the paralysis results from a lesion in the brain the increased reflexes which strychnin causes will serve to delay muscular atrophy. It may also serve to restore the tone of the reflexes when these are lowered by functional disturbances of the cord. Thus incontinence of feces and urine may be relieved when these are due to the lowered reflex centers for the sphincters of the bladder and anus.

Caffein is closely related to strychnin, to which, however, it is greatly inferior, so far as any influence on the circulation is concerned. It stimulates the vasomotor and respiratory centers and is useful, therefore, in the treatment of poisoning by morphin and other narcotics, in the form of strong tea, but strychnin serves the same purpose and perhaps more efficiently.

Hoffmann noticed that theobromin possessed a stimulant action on the myocardium, similar to that shown by caffein, but no vasoconstrictor effect. In therapeutic doses of either agent, however, this cardiac effect is of little importance.

ATROPIN.

Atropin causes acceleration of the heart by paralyzing the vagus endings, and this also causes an increased systole and a lessened diastole. The rate of the heart may be twice as great as under normal conditions, the result being a considerable increase in the output of the heart in a unit of time.

The effect on the circulation of the increased heart action is supplemented by the constriction of the arterioles of the splanchnic area, due to stimulation of the vasoconstrictor area, due to stimulation of the vasoconstrictor center by atropin, which also stimulates the vasodilator center for the vessels of the skin, particularly those of the face and neck, but this is of comparatively little influence on the general blood pressure which rises in response to the two actions just mentioned.

The influence of atropin on the heart rate is much less in children and in old age than it is between the ages of 20 and 60 years, because the vagus inhibition is slight at the extremes of life in man. The vagus is much more active in some animals than in others. In this respect the dog resembles man.

Atropin may cause a brief but unimportant slowing of the heart, due to stimulation of the center, preceding the acceleration which depends on the paralysis of the vagus endings. While it has been undeniably shown that atropin may powerfully stimulate the myocardium, this effect with therapeutic doses is so slight that it may be entirely disregarded. Atropin acts as a stimulant to the respiratory center, but it is inferior in this re-

spect to strychnin; it increases the rate, and probably the depth, of the respiration.

The central action of atropin is exerted mainly on the motor area, but it has been suggested that the differences between the action of atropin, caffein and strychnin on the various parts of the central nervous system are in degree rather than in kind. Thus, while caffein acts mainly on the higher centers in man, stimulating the psychic functions, it is capable of causing strychnin-like convulsions in the frog. All three act as powerful respiratory stimulants in mammals.

Atropin is official as:

ATROPINA.—U. S. P.—Atropin is an alkaloid prepared from *Atropa Belladonna,* or from other plants of the same family. It is soluble in 450 parts of water and in less than 2 parts of alcohol.

ATROPINÆ SULPHAS.—U. S. P.—This salt of atropin is official in many, if not all, pharmacopeias and is the best known and most widely used preparation of the atropin group. It is soluble in less than 1 part of water and in 4 parts of alcohol:

Average dose (alkaloid or salt): 0.0004 gm. (0.4 mg. or 1/160 gr.).

Atropin is indicated when the heart is considerably slowed. For this purpose the average dose given above is not usually sufficient, about 1 mg. (1/65 grain) being necessary to increase the rate; so large a dose being necessary to produce paralysis of the vagus endings in the heart. It must be remembered, however, that in children and in the very old (after 70) the effect to be expected is much less than that seen between the ages of 20 and 60. This larger dose causes stoppage, or, at

least, a marked diminution of salivary secretion with consequent dryness of the mouth and throat.

While atropin has been used in shock and collapse, it can have but little influence on blood pressure or respiration in such cases. Atropin may be used to determine whether an abnormally slowed or intermittent heart results from central influences or from causes within the heart itself, since it cuts off all impulses from the center arriving through the vagus, but produces no appreciable effect if the cause lies within the heart.

Atropin has been used to prevent the reflex stoppage of the heart occurring at the commencement of anesthesia, but it has been shown that there is no danger of such a catastrophe if the anesthetic is not used in too great concentration.

Poisoning by certain fungi which contain muscarin, while rare, may best be treated with moderate doses of atropin. Pilocarpin is also antagonized in nearly all of its actions by atropin, but the latter does not counteract the cardiac effects of physostigmin, which acts on the myocardium.

The value of atropin in opium poisoning has been much disputed. It seems to possess no advantage over caffein and strychnin in such cases and it has the disadvantage of adding to the depression of the respiratory center if more than a therapeutic dose is given. Clinical experience seems to have abundantly proved that small doses of atropin are corrective for ordinary doses of morphin, and it is almost universally so used.[4]

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4. A widely used combination consists of morphin sulphate 0.015 gm. (¼ grain) and atropin sulphate 0.0004 gm. (1/150 grain) prepared in the form of the now popular hypodermic tablets or dissolved in distilled water sufficient for one dose.

Atropin is usually given hypodermically when the central effects are desired.

CAMPHOR.

In shock or collapse camphor given by the stomach produces a feeling of warmth and probably acts reflexly for the most part. The respiratory and vasomotor centers, as well as the heart muscle, are stimulated, thus causing a rise of blood pressure. The heart is usually slowed and the contraction strengthened. Camphor is almost insoluble in water and only slightly volatile at the body temperature, and its action, therefore, is very uncertain; 0.03 gm. (½ grain) may improve the pulse in some cases, while twenty times as much may be required in others; hence but little reliance can be placed on it in crises, though it is very often effective. The spirit, diluted with water, is frequently used for internal administration. A number of camphor derivatives have been employed from time to time, but they have not been shown to possess any advantages over camphor itself, or one of its more simple preparations.

CAMPHORA.—U. S. P.—Camphor is a white, volatile, solid substance having a crystalline structure and a characteristic aromatic odor and taste. Camphor has been used in the Far East for many centuries, but was not known in Europe until introduced by the Arabians. It is now official in all pharmacopeias.

Average dose: 0.12 gm. (2 grains).

AQUA CAMPHORÆ.—U. S. P.—This is a saturated solution of camphor in distilled water. It is

frequently used as a vehicle for other medical substances.

Average dose: 4 c.c. (2 fluidrams).

SPIRITUS CAMPHORÆ.—U. S. P.—This is a 10 per cent. solution of camphor in alcohol.

Average dose: 1 c.c. (15 minims).

LINIMENTUM CAMPHORÆ.—U. S. P.—This preparation, variously known as camphor liniment and camphorated oil, contains 20 per cent. of camphor dissolved in cottonseed oil. While largely used as a mildly rubefacient local application it is not infrequently used for hypodermic injections or for the internal administration of camphor in the form of an emulsion. The average dose would be about half of that given under spirit of camphor.

Camphor is frequently employed as a diaphoretic, particularly in combination with other agents, because of its stimulation of the vasodilator centers for the cutaneous vessels.

As noted above, camphor water alone has little therapeutic value and is useful mainly as a vehicle for other substances. Camphor may be given in pill form, in capsules or in the form of an emulsion. Probably the best method of administering camphor consists in suspending the finely powdered substance in twenty parts or more of milk. For this purpose from twenty drops to one teaspoonful of the spirit of camphor may be directed to be given in one or two tablespoonfuls of milk.

The several preparations of camphor are commonly employed externally as a mild rubefacient, but the action of camphor when applied in this way is largely, if not entirely, a local one.

MUSK.

MOSCHUS.—U. S. P.—This substance has been used in Europe for several centuries, and in China and other far Eastern countries from time immemorial. The portion that is now official is described as "The secretion from the preputial follicles of *Moschus moschiferus*" (musk deer), an animal which inhabits Thibet and other parts of Central Asia.

Average dose: 0.25 gm. (4 grains).

TINCTURA MOSCHI.—U. S. P.—This represents 5 per cent. of musk in diluted alcohol.

Average dose: 1 c.c. (15 minims).

Musk was brought forward nearly a century ago as a powerful circulatory stimulant, and S. Solis-Cohen recently recommended it as an efficient and dependable remedy when it can be obtained of good quality, but it is extremely expensive and subject to gross adulteration.

Musk probably resembles camphor in its action on the centers and has the advantage of greater solubility in proportion to the amount required.

Castor fiber and sumbul root, which have been recommended as substitutes for musk, are entirely devoid of any such central action as that claimed for the latter.

Musk may be given in capsules, or in some cases the tincture may be preferred.

AMMONIUM PREPARATIONS.

While ammonia, as one of the products of the decomposition of nitrogenous materials, was known from a very early period, the volatile salts of this substance were not available in Europe as

medicines until after the thirteenth century, when Raymundus Lullus first produced ammonium carbonate from urine. The stimulating action of this salt, it is said, was known for many centuries to the Hindoos, and was probably known to the Arabians. It is now official as:

AMMONII CARBONAS.—U. S. P.—This is a white, hard, translucent solid having the characteristic odor of ammonia and a sharp saline taste. The official salt is described as being "a mixture of acid ammonium carbonate and ammonium carbamate."

Average dose: 0.25 gm. (4 grains).

AQUA AMMONIÆ.—U. S. P.—This is an aqueous solution of ammonia containing 10 per cent., by weight, of gaseous ammonia.

Average dose: 1 c.c. (15 minims).

SPIRITUS AMMONIÆ AROMATICUS.—U. S. P.—This is a hydroalcoholic solution containing 3.4 per cent. of ammonium carbonate, 9 per cent. of ammonia water and 70 per cent. of alcohol aromatized with oil of lemon, oil of lavender flowers, and oil of nutmeg.

Average dose: 2 c.c. (30 minims).

The volatile salts of ammonium, in the form of the well-known "smelling salts," are very commonly employed by inhalation for their reflex effects on the respiratory and cardiac centers. The aromatic spirit of ammonia when taken by the stomach has a similar action. Other actions of ammonium salts have been enumerated in previous chapters.

The water of ammonia, when taken internally, merely acts as a caustic alkali. It is seldom so

spect to strychnin; it increases the rate, and probably the depth, of the respiration.

The central action of atropin is exerted mainly on the motor area, but it has been suggested that the differences between the action of atropin, caffein and strychnin on the various parts of the central nervous system are in degree rather than in kind. Thus, while caffein acts mainly on the higher centers in man, stimulating the psychic functions, it is capable of causing strychnin-like convulsions in the frog. All three act as powerful respiratory stimulants in mammals.

Atropin is official as:

ATROPINA.—U. S. P.—Atropin is an alkaloid prepared from *Atropa Belladonna,* or from other plants of the same family. It is soluble in 450 parts of water and in less than 2 parts of alcohol.

ATROPINÆ SULPHAS.—U. S. P.—This salt of atropin is official in many, if not all, pharmacopeias and is the best known and most widely used preparation of the atropin group. It is soluble in less than 1 part of water and in 4 parts of alcohol:

Average dose (alkaloid or salt): 0.0004 gm. (0.4 mg. or 1/160 gr.).

Atropin is indicated when the heart is considerably slowed. For this purpose the average dose given above is not usually sufficient, about 1 mg. (1/65 grain) being necessary to increase the rate; so large a dose being necessary to produce paralysis of the vagus endings in the heart. It must be remembered, however, that in children and in the very old (after 70) the effect to be expected is much less than that seen between the ages of 20 and 60. This larger dose causes stoppage, or, at

least, a marked diminution of salivary secretion with consequent dryness of the mouth and throat.

While atropin has been used in shock and collapse, it can have but little influence on blood pressure or respiration in such cases. Atropin may be used to determine whether an abnormally slowed or intermittent heart results from central influences or from causes within the heart itself, since it cuts off all impulses from the center arriving through the vagus, but produces no appreciable effect if the cause lies within the heart.

Atropin has been used to prevent the reflex stoppage of the heart occurring at the commencement of anesthesia, but it has been shown that there is no danger of such a catastrophe if the anesthetic is not used in too great concentration.

Poisoning by certain fungi which contain muscarin, while rare, may best be treated with moderate doses of atropin. Pilocarpin is also antagonized in nearly all of its actions by atropin, but the latter does not counteract the cardiac effects of physostigmin, which acts on the myocardium.

The value of atropin in opium poisoning has been much disputed. It seems to possess no advantage over caffein and strychnin in such cases and it has the disadvantage of adding to the depression of the respiratory center if more than a therapeutic dose is given. Clinical experience seems to have abundantly proved that small doses of atropin are corrective for ordinary doses of morphin, and it is almost universally so used.[4]

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4. A widely used combination consists of morphin sulphate 0.015 gm. (¼ grain) and atropin sulphate 0.0004 gm. (1/150 grain) prepared in the form of the now popular hypodermic tablets or dissolved in distilled water sufficient for one dose.

Atropin is usually given hypodermically when the central effects are desired.

CAMPHOR.

In shock or collapse camphor given by the stomach produces a feeling of warmth and probably acts reflexly for the most part. The respiratory and vasomotor centers, as well as the heart muscle, are stimulated, thus causing a rise of blood pressure. The heart is usually slowed and the contraction strengthened. Camphor is almost insoluble in water and only slightly volatile at the body temperature, and its action, therefore, is very uncertain; 0.03 gm. (½ grain) may improve the pulse in some cases, while twenty times as much may be required in others; hence but little reliance can be placed on it in crises, though it is very often effective. The spirit, diluted with water, is frequently used for internal administration. A number of camphor derivatives have been employed from time to time, but they have not been shown to possess any advantages over camphor itself, or one of its more simple preparations.

CAMPHORA.—U. S. P.—Camphor is a white, volatile, solid substance having a crystalline structure and a characteristic aromatic odor and taste. Camphor has been used in the Far East for many centuries, but was not known in Europe until introduced by the Arabians. It is now official in all pharmacopeias.

Average dose: 0.12 gm. (2 grains).

AQUA CAMPHORÆ.—U. S. P.—This is a saturated solution of camphor in distilled water. It is

frequently used as a vehicle for other medical substances.

Average dose: 4 c.c. (2 fluidrams).

SPIRITUS CAMPHORÆ.—U. S. P.—This is a 10 per cent. solution of camphor in alcohol.

Average dose: 1 c.c. (15 minims).

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The water of ammonia, when taken internally, merely acts as a caustic alkali. It is seldom so

used. The aromatic spirit is usually added to water at the moment of taking.

Smelling salts consist of varying mixtures of ammonium carbonate, or of ammonium chlorid with potassium carbonate, and spirit of ammonia, to which oil of lavender flowers is usually added as an aromatic.

ALCOHOL AND DERIVATIVES.

Alcohol has been considered under dietetics, Chapter VII, and it will be mentioned here only so far as it affects the circulation.

Small doses increase the pulse rate slightly by direct action on the cardiac muscle, and reflexly also, from the stomach if the alcohol has been taken in a concentrated form. Large doses decrease the rate by a stimulation of the vagus.

The dilation of the vessels of the skin is a matter of very common observation. This leads to a fall of temperature, even though it gives rise to a feeling of warmth in the skin. The general blood pressure rises somewhat after small doses, but falls after large amounts.

Alcohol, or distilled spirit, was probably introduced into Europe by the Arabians in the tenth or eleventh century.[5] Apart from the several forms of alcohol that are official we have:

SPIRITUS FRUMENTI.—U. S. P.—An alcoholic liquid obtained by the distillation of the mash of fermented grain, such as Indian corn, rye, wheat and barley, or their mixtures. To conform with the official requirements, whisky should be at least

5. According to Pereira the Arabians obtained their knowledge of distilled spirit from the Chinese, who knew and used it at a much earlier period.

four years old and comply with a number of physical requirements and chemical tests that are now provided.

SPIRITUS VINI GALLICI.—U. S. P.—Brandy. This is an alcoholic liquid obtained by the distillation of the fermented unmodified juice of fresh grapes. Like whisky, it should be at least four years old and should conform to the tests for identity and purity that are described in the Pharmacopeia.

ÆTHER.—U. S. P.—Ether or ethyl oxid was discovered by Valerius Cordus, about 1540, and described as "Oleum vitrioli dulce." The preparation appears to have been entirely forgotten and was rediscovered by Frobenius, a London apothecary, about 1730.

Sulphuric ether, the name given it at the time, although long known to be a misnomer, is still retained in connection with commercial varieties of the substance.

Average dose: 1 c.c. (15 minims).

SPIRITUS ÆTHERIS.—U. S. P.—This contains 32.5 parts of ether and 67.5 parts of alcohol.

Average dose: 4 c.c. (1 fluidram).

SPIRITUS ÆTHERIS COMPOSITUS.—U. S. P.—This preparation, more popularly known as Hoffmann's anodyne, contains 2.5 per cent. of ethereal oil, in addition to the ether. It has no evident advantages over the simple spirit of ether and may be given in the same dose.

Alcohol in the form of whisky or brandy is much used in shock or collapse in connection with other agents, such as strychnin and digitalis. Its

value is strongly asserted by some authorities and disputed by others. Ordinary doses of alcohol have little effect on the circulation in animals, but clinical evidence seems to prove that alcohol does possess some value in the conditions mentioned, particularly when a very brief respite for the heart tides over a crisis. Spirit of ether may be given by the stomach, or used by hypodermic injection, and probably acts reflexly on the centers in such cases.

ERGOT.

Ergot has been recommended in shock and in hemorrhage in inaccessible locations. The use in the latter condition is based on its undoubted power of causing vasoconstriction in certain areas. It is much less useful than strychnin in shock because of its slow action, and in hemorrhage there is no reason to expect a greater vasoconstriction at the bleeding point than elsewhere and a rise in the general blood pressure beyond that necessary to sustain the circulation in the medulla, is contraindicated in hemorrhage. This, of course, does not apply to postpartum hemorrhage, because ergot has a specific action on the uterus, causing a firm contraction and thereby closing the bleeding vessels by compression.

Sollmann and Brown have recently studied the action of ergot when injected intravenously into dogs.[6] They found that it influenced the general circulation but little, particularly when the blood pressure was much lowered, and that it caused a temporary fall in the blood pressure with speedy

6. THE JOURNAL A. M. A., July 22, 1905, p. 229.

recovery, generally followed by an unimportant rise. The effects were mainly due to the action on the heart, as the vasomotor action was very slight.

The further discussion of its obstetrical use does not belong here.

ERGOTA.—U. S. P.—The sclerotium of *Claviceps purpurea,* gathered from rye, and not more than one year old.

While ergot has been used in Germany for centuries as a household remedy, it was not generally recognized as an efficient drug until some time after 1777, when Desgranges published several essays on the use of ergot.

The vasoconstrictor properties of this drug appear to be due to the alkaloid cornutin, discovered by Kobert in 1884, and more fully described by Keller in 1894.

EXTRACTUM ERGOTÆ.—U. S. P.—This is a hydroalcoholic extract of ergot partially purified by the addition of hydrochloric acid subsequently neutralized with sodium carbonate. It should represent eight times its weight of ergot.

Average dose: 0.25 gm. (4 grains).

FLUIDEXTRACTUM ERGOTÆ.—U. S. P.—This is directed to be made with diluted alcohol that has been acidified by the addition of acetic acid.

Average dose: 2 c.c. (30 minims).

VINUM ERGOTÆ.—U. S. P.—This represents 20 per cent. of the fluidextract of ergot in fortified white wine.

Average dose: 8 c.c. (2 fluidrams).

Ergot is preferably given in the form of the fluidextract without other additions. There are a number of water-soluble preparations on the market at the present time that are intended for hypodermic use, which, it is claimed, possess all the active principles of ergot, without the odorous and nauseating constituents.

CHAPTER XV.

CIRCULATORY DEPRESSANTS.

The circulation may be depressed by acting on those structures the stimulation of which causes an increase in blood pressure. Hence we might divide these agents into two groups: 1. Those acting on the heart mainly, directly or through the centers. 2. Those acting for the most part on the vessels, directly or indirectly.

An agent which slows the heart without causing a compensating increase in the strength or the amplitude of the contraction, or a constriction of the vessels, must cause a fall in the arterial pressure, as will be readily understood by reference to what has previously been said in regard to acceleration of the heart causing a rise in pressure. Here, too, we have in every case a combination of effects, and the resulting change in the circulation must depend on the predominance of one or another. As a matter of fact, we have no circulatory depressant which is used therapeutically to slow the heart by direct action on the myocardium, but there are a number which induce slowing by indirect action.

ACONITE.

Therapeutic doses of aconite cause slowing of the heart by stimulating the vagus center, without materially affecting the strength of the individual contractions or the condition of the vaso-

motor center. The result, therefore, is a fall in arterial pressure.

The lessened cardiac action is accompanied by a decline in the temperature, whether this was previously normal or that of fever. The effect is commonly ascribed to the change in the circulation, but it has not been proved that the heat regulating center is not involved in the action.

It will be noticed that the effects of digitalis and aconite on the circulation are diametrically opposed, except for the slowing of the pulse rate, which both induce.

Toxic doses of aconite act directly on the heart, causing acceleration with diminished force of contraction. In mammals the acceleration is prevented for a time by the vagus stimulation, and the heart is actually slowed, but in reality only a therapeutic dose has been absorbed in the early stage of the action; this stimulation rapidly gives place to depression and then to paralysis of the center, the acceleration becoming marked and being soon followed by great irregularity. Delirium cordis occurs before the heart stops in diastole.

Paralysis of the respiratory center is usually the immediate cause of death; hence atropin is capable of saving a certain percentage of animals experimentally poisoned with a barely fatal dose of aconite. If an excessive dose has been taken even artificial respiration will prolong life only for a short time, as the heart soon becomes paralyzed after the phenomena enumerated above.

ACONITUM.—U. S. P.—This is the dried tuberous root of *Aconitum napellus,* collected in autumn. When assayed by the process given in the

Pharmacopeia it yields not less than 0.5 per cent. of aconitin.

Despite the fact that it was well known and long in use as a poison, particularly for wild animals, aconite is a comparatively recent addition to our materia medica, having been introduced by an Austrian physician, Störck, about 1762.

Average dose: 0.05 gm. (1 grain).

The official preparations of aconite are as follows:

FLUIDEXTRACTUM ACONITI.—U. S. P.—This is made with a mixture of 75 parts of alcohol and 25 parts of water and should contain 0.4 per cent. of aconitin.

Average dose: 0.05 c.c. (1 minim).

TINCTURA ACONITI.—U. S. P.—This preparation has been materially reduced in strength and now represents 10 per cent. of the crude drug, or approximately one-third of the strength of the tincture that was official in the Pharmacopeia for 1890.

It may be added that the change was made in conformity with the recommendations of the international conference for the unification of formulas of potent medicaments and that, in addition to being in harmony with this international standard it will be found to be more uniformly active than the stronger but more variable tincture official in the earlier pharmacopeias.

Average dose: 0.6 c.c. (10 minims).

ACONITINA.—U. S. P.—This is an alkaloid obtained from aconite. It is the most active and most potent substance in the Pharmacopeia. The aconitin now official is the crystalline alkaloid and

motor center. The result, therefore, is a fall in arterial pressure.

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ACONITINA.—U. S. P.—This is an alkaloid obtained from aconite. It is the most active and most potent substance in the Pharmacopeia. The aconitin now official is the crystalline alkaloid and

should not be confounded with the amorphous substance formerly official or the comparatively weak eclectic preparation of aconite.

Average dose: 0.00015 gm. (0.15 mg. or 1/400 grain).

Aconite finds its greatest usefulness in cases of high blood pressure with a strong, rapid heart, particularly in fever in robust persons. It then simply slows the heart, lessening its output and causing a fall in temperature and in arterial tension.

Fever alone is not an indication in every case for the use of aconite. In continued fevers and in any case in which the heart is feeble or the arterial tension low from any cause (even though the pulse may be rapid), aconite is contraindicated.

Since the antipyretic benzene derivatives have come into general use the employment of aconite in fever has correspondingly declined, but we have seen that the synthetic antipyretics are far from being the harmless substances that some of the manufacturers would have us believe, and aconite deserves to be used more frequently in suitable cases of fever.

"Colds" are troublesome forms of congestion resulting from circulatory disturbances which are often relieved by repeated small doses of aconite. For this purpose 3 drops (about 1 minim) of the tincture of aconite of the present Pharmacopeia, which would be equivalent to about 1 drop (1/3 minim) of the tincture official in the Pharmacopeia, 1890, well diluted with water, may be given every fifteen minutes for two hours, then hourly until relief is obtained.

Aconitin is so intensely irritant that it is not suitable for use without great dilution, and, as there is some chance of confusing the much more potent article now official with the eclectic or the amorphous preparations, it will be found preferable to use the tincture of aconite in nearly every case, more particularly, since this is now required to be of a definite aconitin strength. Because of its irritant action aconitin is not adapted for hypodermic use, but it may be given, largely diluted with water, as follows:

Aquæ, q. s. ad	f℥iv	120
Alcohol	f℥iv	15
Aquæ, q. s. ad	f℥iv	120

Sig.: A teaspoonful may be taken every three hours.

The disadvantage, not to say danger, of trying to weigh such small amounts is apparent, and serves to further illustrate the advantage of using the tincture.

The tincture is usually given alone, except for the water used in diluting it.

VERATRUM.

Veratrum rather closely resembles aconite in its therapeutic action, and it was widely used at one time for the reduction of fever. The extent of its use was largely due to its popularization in the form of Norwood's Tincture of Veratrum, but it seems to possess no advantage over aconite, and it is now but seldom used internally.

VERATRUM.—U. S. P. (VERATRUM VIRIDE.—U. S. P., 1890).—Under the single heading veratrum, the Pharmacopeia now recognizes the dried rhizome of *Veratrum viride* or of *Veratrum album.* While it is true that there is no marked difference

the value of amyl nitrite in angina pectoris that the coronary vessels, like those of the face and brain, may be dilated at first, before the action on the general circulation begins. Filehne showed that the therapeutic dose of amyl nitrite caused vasodilatation by central action, and Loeb found it did not affect the vessel tonus independently except when in such concentration as to prove poisonous. Small doses were found to have no constant effect on the vessels of the coronary circulation in the excised heart. Amyl nitrite acts very rapidly when inhaled, but the action is over in about twenty minutes.

The effects of glyceryl trinitrate or nitroglycerin are much more slowly induced and they persist for some hours. Sodium nitrite is decomposed by the hydrochloric acid of the gastric juice, thus giving rise to irritation of the stomach. Glyceryl trinitrate is not decomposed in the stomach, but it has the disadvantage of often causing headache. In some cases this action does not occur after the drug has been used for some time. Glyceryl trinitrate is decomposed in the blood, with the liberation of the nitrous acid radicle; hence it acts like the nitrites.

SPIRITUS GLYCERYLIS NITRATIS.—U. S. P. (SPIRITUS GLONOINI.—U. S. P., 1890)—Commonly, though incorrectly, termed nitroglycerin, is an alcoholic solution containing 1 per cent. by weight of glyceryl trinitrate.

Average dose: 0.05 c.c. (1 minim).

AMYLIS NITRIS.—U. S. P.—This is a liquid containing about 80 per cent. of amyl nitrite.

Average dose: 0.2 c.c. (3 minims).

SODII NITRIS.—U. S. P.—This usually occurs in white, or nearly white, fused masses, soluble in less than two parts of water. The salt deliquesces on exposure to air and is also gradually oxidized to sodium nitrate and thus becomes unfit for use.

Average dose: 0.06 gm. (1 grain).

The nitrites, and glyceryl trinitrate, are of prime importance in the depression of the circulation and may be used when it is deemed necessary to lower the blood pressure, for example, when a weakened heart is becoming exhausted by contracting against a great arterial resistance, and the contractions are incomplete, as in arteriosclerosis. A slight lowering of the aortic resistance often enables the heart to contract more perfectly while a coronary vasodilation secures a better nutrition of the heart.

The group is contraindicated, however, when the blood pressure is already low (however weak and rapid the heart may be), because a certain degree of arterial tension is absolutely essential for maintaining the coronary and medullary circulations.

Amyl nitrite is to be preferred when a speedy action is desired, as in acute attacks of angina pectoris. When the constriction of the vessels is of spasmodic origin the nitrites usually give relief, but in the later stages of arteriosclerosis, when most of the muscular tissue has been replaced by fibrous, thus narrowing the lumen of the vessels, it is obvious that such vessels can not be caused to dilate by any means.

It must not be forgotten that, while relief is often obtained in the acute attacks of the early

stages of angina pectoris, the nitrites are merely palliative and in no sense curative. The nitrites, and more particularly amyl nitrite, are indicated in vasomotor spasm occurring in any disease, unless specifically contraindicated by other conditions.

The action of amyl nitrite is very speedily elicited when it is inhaled, but when spasm of the respiratory muscles interferes with the inhalation it may be injected into the deep muscles of the thigh.

Spirit of glyceryl trinitrate is to be preferred in chronic conditions of abnormally high blood pressure, because of its more protracted action. One minim is given three times a day, or the dose is increased till effective. It may be injected hypodermically or given by the stomach, as it passes through that organ unchanged, and, therefore, causes no such disturbances as are seen with sodium nitrite.

While this substance is usually considered as being extremely poisonous, it is said that large amounts have been given in the course of a day with no bad effects. Aqueous solutions of glyceryl trinitrate are unstable and are frequently quite worthless. The spirit sometimes gives almost immediate relief in headache, when this is attended with high blood pressure, but, on the other hand, it may increase the headache if the blood pressure is low. As is well known, the headache which glyceryl trinitrate commonly causes is one of the greatest objections to its use.

The nitrites, and particularly the spirit of glyceryl trinitrate, may be used to counteract the

vasoconstrictor effect of digitalis or strychnin when that action is undesired.

Spirit of nitrous ether does not yield enough of the nitrous acid radicle to exert any therapeutic action on the circulation. The action of the spirit is exerted reflexly as in the case of alcohol and ether.

The spirit of nitroglycerin may be given in simple solution in order to avoid the measuring of such small does as one minim. It may be prescribed as follows:

℞.	Spiritus nitroglycerini	m. xv	1
	Aquæ	f℥ii	60

The dose of this solution is a teaspoonful. Large amounts should not be prescribed or dispensed.

The following illustrates the method of prescribing sodium nitrite:

℞.	Sodii nitritis	gr. xv	1
	Aquæ dest.	℥ii	60

This solution should be kept well corked. The dose is one teaspoonful.

The well-known "pearls" of amyl nitrite afford the most convenient form for dispensing that substance; they must be kept cool to avoid loss by breakage, and, when used, one is crushed in a handkerchief and the contents inhaled by the patient at once.

Bloodletting was formerly in vogue as a routine procedure when it was desired to reduce the blood pressure, but in healthy animals the vasomotor center exercises such perfect control over the blood pressure that the loss of blood produces very little lasting effect unless it is so great as to cause col-

lapse symptoms. While the loss of a moderate amount of blood is well borne by robust patients, and in some cases may even prove beneficial, aconite and the nitrites are nearly always to be preferred as temporary measures, while the control of the diet (including liquids) and the use of saline purgatives will serve to diminish the amount of blood for a longer time in suitable cases.

Hydrated chloral is one of the most effective agents in our possession for lowering the blood pressure by depressing the vasomotor centers, and, while this action is much employed in laboratory experiments, it is not elicited in man by perfectly safe doses such as are used to induce sleep.

CHAPTER XVI.

DIURETICS AND DIAPHORETICS.

Diuretics and diaphoretics may be considered together, since they are often used for the same purpose, the one being used to supplement the other, and because the same agent which produces diuresis under certain conditions may cause diaphoresis when these conditions are slightly changed.

Diuretics may be divided broadly into those which influence the circulation and those which act on the secretory cells of the kidney. Though the same agent may possess both actions to some extent, we shall consider these remedies with reference to the principal effect according to this classification.

While the exact mechanism of urinary secretion remains a problem, the indications for diuresis and the method of causing it are fairly clear. When the official remedies all fail to produce this effect we may usually attribute the failure to the condition of the kidney, feeling sure that the secretory cells are incapable of performing their function and that nothing short of the creation of new cells can be effective. Even this task is not beyond the powers of some of the much-vaunted mineral waters and nostrums if we are to believe the statements made in the circulars and other advertisements of the proprietors.

Diuretics are especially indicated in dropsy of

cardiac, or even of renal, origin, provided the cells are capable of free secretion. In renal dropsy agents of the first class (those which influence the circulation), or those which mildly stimulate the kidney cells without producing irritation, are to be preferred. If the renal cells are incapable of increased secretion, diaphoresis should be resorted to in order to give rest to the kidneys.

Diuretics are also important in causing the removal of toxins and substances which form concretions (urates and phosphates).

DIGITALIS.

Nearly all authorities agree that digitalis is the most important of the official remedies in the treatment of dropsy of cardiac origin, its action being directed mainly toward the increase in the efficiency of the heart, with a consequently improved circulation in the kidney and increased diuresis. For this purpose the tincture is frequently employed, but, perhaps, the most efficient remedy is the combination of digitalis with squill and calomel, commonly called Niemeyer's pills.[1]

The official squill is too irritant to permit of its employment in nephritis. This is very important and should be borne in mind if one uses any of the much-heralded diuretic nostrums which contain squill or its active principles.

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1. The formula for this pill is as follows:

Pulveris digitalis	
Pulveris scillæ, āā.....grs. x	60
Hydrarg. chloridi mit.....grs. 1 ¼	08

This amount is to be divided into ten pills, or preferably, capsules. One of these pills every three hours will be found effective. The calomel is often omitted, or it may be replaced by 0.06 gm. (1 grain) of the blue mass (massa hydrargyri) in each dose, if it is to be made into pills, or gray powder (hydrargyrum cum creta), if into capsules.

That squill is extremely active in causing a watery diuresis is true, but in overdoses it is equally potent to lessen or even to suppress the flow by reason of its irritant action. This may result in bloody urine.

The dose of squill, in powder, is 0.05 to 0.1 gm. (one or two grains) every three hours until some nausea occurs.

Rather closely resembling digitalis in its action on the heart and as a diuretic, if, indeed, it may not surpass the older drug in the latter case, is strophanthus, which does not cause the same degree of vasoconstriction which sometimes interferes with or prevents the diuretic action of digitalis. It is mostly used in the form of the tincture.

While strophanthus has some advantages, such as the more prompt action and a slighter tendency to cause cumulative effects, clinicians have not found it so generally useful as digitalis.

Apocynum has enjoyed a considerable reputation in domestic practice as a remedy in dropsy, but appears to be inferior to digitalis in the same group with which it belongs.

Digitalis, strophanthus, apocynum and other members of this group have been considered in Chapter XIV.

CAFFEIN.

When cardiac stimulants or other agents cause such vasoconstriction as greatly to lessen the amount of blood which passes through the kidney, and consequently the diuresis, a vasodilator is sometimes employed, but it is more rational to avoid the necessity for this when possible.

When the object of diuresis is to get rid of fluid which has accumulated, it is, of course, better to avoid unnecessary amounts of water, and in such cases diuretics are given in solid, or at least concentrated, form.

Caffein, theobromin, para-xanthin and theocin are derived from xanthin by the introduction of methyl groups, caffein being trimethylxanthin, and theobromin, para-xanthin, and theocin being dimethylxanthins, the last three differing only in the arrangement of the methyl groups in the molecule. These dimethylxanthins act more strongly on the muscles of the vessels and cause a greater diuresis than does caffein, while the latter acts more energetically on the centers, causing greater wakefulness and greater stimulation of vasomotor and respiratory centers.

Therapeutic doses of caffein increase the heart rate somewhat by acting directly on the musculature; the force is changed but little, being slightly increased, resulting in an increased output in a unit of time; this, with the stimulation of the vasomotor center, causes a rise of blood pressure. The vasoconstriction at first may interfere with diuresis, despite the increased blood pressure, but the vasoconstriction is transient and in about twenty minutes it is succeeded by a slight dilation of the vessels of the kidney, while the general blood pressure remains a little above normal and the diuresis is increased. Caffein is supposed to stimulate the renal epithelium, causing a considerable increase in the secretion of the watery part of the urine, but not so great an increase in the solid portion; hence the specific gravity of the

urine falls. Caffein is said to bring about a dilation of the vessels by a direct action on the walls.

The effect of caffein on the psychic centers is a matter of common observation. Small doses result in an increased capacity for mental work, particularly noticeable after the centers have had a short rest, as after a brief sleep. It lessens the feeling of fatigue and increases the capacity for physical work after a period of rest, but not when it is taken during exhaustion or very severe fatigue. Tea and coffee owe their stimulating effects, in part, to the volatile oils which they contain and which are dissipated by boiling.

Caffein is a constituent of tea, coffee, kola, and, more abundantly (5 per cent.), of guarana, which is official.

Caffein is not very soluble in water or alcohol, but its solubility in water is greatly increased by such salts as potassium bromid and sodium benzoate or salicylate; this well-known fact has been appropriated as a "discovery" by manufacturers of certain nostrums.

Caffein is most effective when given in the form of hot tea or coffee, the effect being heightened by certain volatile oils present and by the reflex stimulation of the hot fluid in the stomach. Tea made by quick extraction contains but little tannin and does not disturb digestion to the same extent as that made by long contact of the water with the leaves. Caffein (and particularly hot tea) is useful as an antidote to such narcotic poisons as morphin and alcohol, and it is also added to the antipyretics to lessen central depression.

Diuresis serves to remove certain toxins which

are excreted by the kidneys, and a copious watery diuresis may serve to lessen the action of such metals as mercury and lead.

Diuretics are useful in dropsy, and, since the object is the removal of liquid, caffein, digitalis, theobromin and those which are used with but little water are to be preferred in such cases.

Digitalis is used in the form of the tincture, or more frequently, perhaps, as an infusion. Caffein may be given in the form of hot tea or coffee. If the former made quickly, removed from the leaves and the clear infusion then boiled, the volatile oils are dissipated. This may be advantageous when it is desired to minimize the wakefulness which tea causes. One of the soluble forms of caffein suggested below may be used if preferred.[2] Theobromin may be given in the form of hot cocoa.

When digitalis or other diuretics produce a more than temporary vasoconstriction in the kidney, one drop of the 1 per cent. solution of nitroglycerin may be given at the same time.

Caffein Sodio-Benzoate, N. F., and Caffein Sodio-Salicylate, N. F., consist of 50 per cent. of caffein, with sodium benzoate and sodium salicylate, respectively.

CAFFEINA.—U. S. P.—This is a feebly basic (alkaloidal) substance obtained from *Thea sinen-*

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2. The following mixture, to be varied according to needs, represents the method of using caffein in this soluble form:

Caffein (alkaloid)		
Sodium salicylate, each	ʒi	4
Cinnamon water to make	℥iii	100

Each teaspoonful contains about 0.2 gm. (3 grains) of caffein. Sodium benzoate or lithium salicylate or benzoate may be substituted for the sodium salicylate. This formula requires no unusual pharmaceutical skill to compound and the cost is very much less than that of the proprietaries used for the same purpose.

sis, Coffea arabica or other plants. It does not form stable salts.

Average dose: 0.05 gm. (5.0 mg. or 1 grain).

The other soluble forms of caffein are:

CAFFEINA CITRATA.—U. S. P.—This consists of equal parts of caffein and citric acid.

Average dose: 0.1 gm. (2 grains).

CAFFEINA CITRATA EFFERVESCENS.—U. S. P.—This contains 4 per cent. of citrated caffein.

Average dose: 4 gm. (60 grains).

Diuretin is a trade name applied to a mixture of theobromin-sodium and sodium salicylate, while agurin consists of theobromin-sodium and sodium acetate. Diuretin and agurin are decomposed on exposure to the air and become much less soluble.

The official sugar of milk and the unofficial urea cause diuresis, probably by acting on the renal epithelium.

SCOPARIUS.—U. S. P.—This is sometimes incorrectly classed with digitalis because it slows the heart, but it weakens the beat, while digitalis strengthens it. The alkaloid, spartein, is responsible for the cardiac and vasoconstrictor effect of scoparius, but the diuretic effect is due to scoparin, a glucosid.

Average dose (of scoparius): 1 gm. (15 grains).

The infusion or decoction is recommended for producing diuresis, except in dropsy.[3]

SPARTEINÆ SULPHAS.—U. S. P.—While this is obtained from scoparius, it is not a true diuretic,

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3. **Soparius**
Potassium bitartrate, each.....℥ss 15

This quantity of material is to be added to 1 liter (1 quart) of water, in a suitable vessel, boiled for ten minutes, allowed to cool and strained. A wineglassful of the resulting decoction may be given every hour.

and it is also of little or no value as a circulatory stimulant.

Average dose: 0.01 gm. (1/5 grain), but this dose is sometimes considerably exceeded.

IRRITANTS.

Irritants which are excreted by the kidneys produce diuresis, but, of course, they must not be used in greater amounts than are necessary to produce a mild stimulation. They are contraindicated in nephritis.

The use of calomel in connection with squill and digitalis has been mentioned. It is most useful in cardiac dropsy and its use is to be stopped when the diuresis becomes free. It may be given in dose of 0.2 gm. (3 grains) daily, or in the form of Niemeyer's pills, combined with digitalis and squills.

VOLATILE OILS.

The irritants include a number of volatile oils which are much more frequently used for their antiseptic action on the urinary tract than for any slight increase in renal action which they may cause. They include such volatile oils as oil of turpentine and oil of juniper, which are more often used as diuretics than copaiba, cubeb and matico, which are employed mainly as antiseptics.

HEXAMETHYLENAMIN.

The volatile oils have been largely superseded as urinary antiseptics by the now official hexamethylenamin.[4]

4. The official name is very cumbersome, but no satisfactory substitute has thus far been suggested. Hexamethylenamin was first brought before the profession by Schering under the trade name of urotropin (Schering & Glatz), and it is still sold by them under this name. It is also on the market under various other trade names, such as formin aminoform, cystogen and others.

HEXAMETHYLAMINA.—U. S. P.—(Hexamethylen tetramin). This is a condensation product produced by the union of formaldehyd and ammonia. While free from the irritating effect of formaldehyd, it yet retains its antiseptic properties, the formaldehyd being gradually set free by dilute acids. Being an ammonium derivative, a solvent effect on uric acid has been claimed for it, just as for lithium salts. It is readily soluble in water and is best given in solution.

Average dose: 0.25 gm. (4 grains).

This substance has been introduced with some slight modification under various names; usually the modification is only sufficient to enable the manufacturers to say that their product is not identical with the official. For instance, helmitol is anhydromethylen citric acid with hexamethylenamin. Uriform embraces two other drugs of minor importance. The official preparation may be considered at least equal to them, since it is not modified by any useless or inferior products, and its purity is easily insured by chemical tests.

UVA URSI.

Another drug of this class which has been the subject of much dispute is uva ursi. Its principal usefulness is probably in catarrhal conditions of the urinary tract. It contains a glucosid, arbutin, which is decomposed, partly perhaps in the kidney, but more abundantly in contact with catarrhal mucous membrane, hydrochinon, an antiseptic, being formed.

UVA URSI.—U. S. P.—The dried leaves of *Arctostaphylos Uva Ursi*, of which the only official preparation is:

FLUIDEXTRACTUM UVÆ URSI.—U. S. P.

Average dose: 2 c.c. (30 minims).

Infusion of uva ursi is made according to the general formula for infusions by pouring 1 liter (1 quart) of boiling water on 50 gm. (1 oz. 5 dr.) of bruised uva ursi.

The fluid extract or the infusion may be given alone three or four times daily.

CHIMAPHILA.—U. S. P.—The dried leaves of *Chimaphila umbellata,* commonly called pipsissewa. It was introduced in America by Dr. John S. Mitchell in 1803, and later into England.

Its medicinal action closely resembles that of uva ursi, to which, however, chimaphila is inferior.

FLUIDEXTRACTUM CHIMAPHILÆ.—U. S. P.

Average dose: 2 c.c. (30 minims).

There remains to be considered an important class of substances which are used as diuretics, but they are so well known that only a very brief notice is needed here.

SALINE DIURETICS.

When diffusible salts of the alkalies are absorbed into the blood they increase the amount of fluid and thereby increase diuresis and diaphoresis.

The acetates are converted into carbonates and thus diminish the acidity of the urine or even render it alkaline.

When the alkaline carbonates are given by the mouth they neutralize the gastric juice and interfere with digestion, but this does not occur with the acetates and citrates. The sulphates are not readily absorbed from the alimentary canal and

usually they do not cause diuresis when given by the mouth. Potassium nitrate is a very effective diuretic, but it causes some gastric irritation.

The official salts most commonly employed as diuretics are:

POTASSII ACETAS.—U. S. P.
Average dose: 2 gm. (30 grains).
POTASSII BITARTRAS.—U. S. P.
Average dose: 2 gm. (30 grains).
POTASSII CITRAS.—U. S. P.
Average dose: 1 gm. (15 grains).
POTASSII NITRAS.—U. S. P.
Average dose: 0.5 gm. (8 grains).
SODII ACETAS.—U. S. P.
Average dose: 1 gm. (15 grains).
SODII CITRAS.—U. S. P.
Average dose: 1 gm. (15 grains).

SALTS OF LITHIUM.

For decades lithia has been a favorite shibboleth for that class of wonder-workers who essay to dissolve uric acid from the hidden recesses of the human body where they believe it to be the causative factor in such widely varying conditions as rheumatism, epilepsy, pneumonia, Bright's disease, migraine and aneurysm.

These claims of the nostrum-makers have resulted in a widespread belief that the salts of lithium, either in large or small quantities, serve as uric acid solvents of unusual potency.

While it is not demonstrable that these salts have any advantages as diuretics over other corresponding salts of the alkali metals, they are, nevertheless, widely used, even at the present time, and

will no doubt continue to occupy a place in our materia medica for some time to come.

It is more than sixty years since Lipowitz announced that this salt favored the solution of uric acid. Since then the lithium salts have been widely used, especially in combination with purgatives and diuretics, but there is no evidence that any benefits result from such combinations.

The lithium salts are of comparatively little importance according to the accepted authorities in therapeutics of to-day.

The official preparations of lithium are:

LITHII CARBONAS.—U. S. P.

Average dose: 0.5 gm. (8 grains).

LITHII CITRAS.—U. S. P.—Is used for the same purposes and in the same dose as the carbonate.

LITHII CITRAS EFFERVESCENS.—U. S. P.—Is a convenient form for administering the citrate.

Average dose: 8 gm. (120 grains).

LITHII SALICYLAS.—U. S. P.

Average dose: 1 gm. (15 grains).

Lithium salicylate was made official in 1880 because of its asserted superiority in the treatment of acute rheumatism; it possesses no advantages over the other salicylates, but the nostrum-makers having seized on it while the first reports of its successful use were being circulated, they continue to make the most extravagant claims for it in their preparations. Cushny specifically denies that this salt has any especial solvent action on uric acid in acute rheumatism.

DIAPHORETICS.

The methods used for producing diaphoresis are analogous to those employed for diuresis, con-

sisting in those which influence the circulation and those acting on the sweat glands; but, in addition, certain agents, notably solution of ammonium acetate, act on the sweat center.

The circulation in the skin is readily influenced by the application of heat in numerous ways and by what amounts to the same thing, the prevention of its loss by an impervious cover, such as oiled silk, or by agents which cause dilation of the vessels of the skin, such as hot alcoholic drinks and spirit of nitrous ether. Everyone is familiar with the sweating of nausea, and, while any nauseant will cause diaphoresis, the only one which is generally employed for this purpose is the powder of ipecac and opium, the well-known Dover's powder. The only official substance used for the purpose which directly stimulates the secretion of sweat is pilocarpus and its alkaloid, pilocarpin. They do not act on the secretory cells, as caffein does on the kidney, but by stimulation of the secretory nerves.

Diaphoretics are employed to arrest "colds" in the early stages, to aid in getting rid of fluid accumulation, as in dropsy, and to a lesser extent for getting rid of secretions. Diaphoresis often serves to relieve the kidneys or to supplement their action. Vegetable infusions which cause diuresis will usually cause diaphoresis at the same time if the patient is kept warm and measures are taken to increase the blood supply of the surface (rubbing, mustard, etc.).

For the arrest of "colds" nearly anything causing sweating seems to be effective, but the powder of ipecac and opium enjoys a particular reputation.

Among the official substances that are more directly useful as diuretics we have:

PULVIS IPECACUANHÆ ET OPII.—U. S. P.—Powder of Ipecac and Opium (Dover's Powder) contains 10 per cent., each, of ipecac, powdered, and powdered opium.

Average dose: 0.500 gm. (7½ grains).

PULVIS MORPHINÆ COMPOSITUS.—U. S. P.—Compound powder of morphin, also known as Tully's powder, containing 1.5 per cent. of morphin and 32 per cent. of camphor, has also been recommended, and is sometimes used, as a diaphoretic, in place of the older and more popular Dover's powder.

Average dose: 0.500 gm. (7½ grains).

Potassium citrate, referred to as a diuretic, is much used for its diaphoretic effect, particularly in the form of:

LIQUOR POTASSII CITRATIS.—U. S. P.—This is an aqueous solution of potassium citrate, containing about 8 per cent. of anhydrous potassium citrate.

Average dose: 15 c.c. (4 fluidrams).

SPIRITUS ÆTHERIS NITROSI.—U. S. P.—Sweet spirits of niter. This is a very generally popular diaphoretic which is also used as a diuretic in fevers.

Average dose: 2 c.c. (30 minims).

LIQUOR AMMONII ACETATIS.—U. S. P.—The old-time spirit of Mindererus.

Average dose: 15 c.c. (4 fluidrams).

The only official drugs which have diaphoresis as their predominant therapeutic action are pilocarpus and its alkaloid, pilocarpin. They are both

too well known to require very extended notice in this place.

Pilocarpin augments the secretion of the sweat and salivary glands and of the gastric mucous glands. It has much less influence on the secretion of milk, bile, pancreatic juice and urine.

The watery constituent of the secretion is increased to a much greater extent than the solid portion is, but the latter are also notably affected. The seat of action is in the nerve endings, and it is antagonized by atropin.

Therapeutic doses of pilocarpin are followed by sweating, which is first seen on the neck and face, and which lasts from three to five hours. Pilocarpin is said to increase the rate of growth of hair, but it, like all other substances, is usually useless in case of baldness. Pilocarpin constricts the pupil by acting on the same structures which atropin affects, having but very little effect on the central nervous system.

Overdoses cause death by asphyxia, due to excessive secretion by the glands of the respiratory passages.

Pilocarpin is the physiologic antagonist of atropin, not because of any diaphoretic action, but because it stimulates the structures which atropin depresses.

PILOCARPUS.—U. S. P.—Pilocarpus or jaborandi leaves contain, by assay, not less than 0.5 per cent. of alkaloids.

Average dose: 2 gm. (30 grains), given occasionally in the form of a 5 per cent. infusion, made according to the official general formula for that class of preparations.

FLUIDEXTRACTUM PILOCARPI.—U. S. P.—This is made with diluted alcohol and contains 0.4 per cent. of the alkaloids from pilocarpus.

Average dose: 2 c.c. (30 minims).

PILOCARPINÆ HYDROCHLORIDUM.—U. S. P., and

PILOCARPINÆ NITRAS.—U. S. P., are therapeutically identical. They are both very soluble in water.

Average dose (either): 0.01 gm. (1/6 grain).

CHAPTER XVII.

CATHARTICS.

Cathartics are among the most ancient of all medicinal agents, rhubarb having been in use among the Chinese for more than forty-five centuries, and senna and aloes were also used in ancient times.

The use of purgatives is so general that it is usually considered a safe and harmless course, even when it does no good. This is true in the vast majority of cases, but Dr. M. L. Harris has recently called attention to the abuse of cathartics in conditions where they are potent for much harm. Among these he mentions: Closure of the intestine, as by strangulated hernia; complete local intestinal paralysis; localized spasmodic constriction, which tends toward spontaneous cure, but demands opium rather than cathartics; appendicitis and peritonitis, in which it is agreed that irritant cathartics, at least, are contraindicated, whatever the individual opinion may be in regard to the use of the salines.

Among the possibilities for the direst harm it may be pointed out that when a portion of the intestinal tract is paralyzed, which may occur in ptomain poisoning, active cathartics might produce intussusception by driving the healthy contracted bowel into the paralyzed relaxed portion.

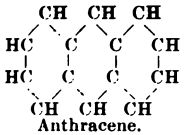
Laxatives, purgatives and drastics will be considered in this chapter. While these three classes

are usually recognized by clinicians, there is no sharp distinction to be drawn between them, as large doses of laxatives or small doses of drastics will act as purgatives.

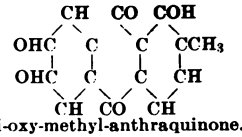
For convenience, rather than evident pharmacologic reasons, we classify cathartics as: Vegetable cathartics, depending for their action on anthracene derivatives; drastics, or the resin anhydrids; purgative oils; laxative sweet substances; saline purgatives; mercurials; bile and miscellaneous purgatives.

THE ANTHRACENE DERIVATIVES.

The graphic formula of anthracene will help to show the relationship existing between several of these derivatives. Anthracene ($C_{14}H_{10}$) consists of three benzene rings united thus:



Anthracene.



Tri-oxy-methyl-anthraquinone.

If an atom of H in the anthracene group is replaced by one of O, the compound is called anthraquinone or anthrachinone. Other atoms of H may then be replaced by OH and the compound is called oxyanthraquinone, a prefix to the *oxy* showing the number of such OH groups in the compound; thus the name tri-oxy-methyl-anthraquinone indicates that four H atoms of anthraquinone have been replaced, three by OH groups and one by a methyl group CH_3. This compound is known as emodin.

Emodin and related compounds are found in all

the drugs which owe their activity to the anthracene derivatives, but the constitution of emodin may vary in the arrangement of the substituted OH groups in different plants. Natal aloes contains no emodin or related compound; hence it is not usually purgative for man, but it is not found in commerce at the present time. Natal aloes is said to act as a purgative for man when the diet consists of meat.

Other members of this group of cathartics contain other principles besides emodin, which are derived from the anthracene nucleus; thus chrysophanic acid, or di-oxy-methyl anthraquinone, is also found in rhubarb, senna, rumex and probably in frangula. The name indicates that there are but two OH groups instead of three, as in the case of emodin.

Chrysophanic acid is too irritant to be used alone as a cathartic. When drugs containing it are taken, it is absorbed too rapidly to exert its action and is excreted in the urine.

After taking rhubarb or senna, the urine is colored yellowish if acid, and purplish if alkaline.

Many other substances, the chemistry of which is obscure, are found in the cathartic drugs.

Preparations of the crude drugs contain colloidal matter which enhances the action of the pure principles, and they are, therefore, to be preferred to the latter; a fact to be remembered when reading the circulars of those nostrum makers who lay stress on their extraordinary facilities for supplying *pure* principles.

The drugs of the anthracene group are characterized by a mildly irritant action whereby they

usually purge in from 8 to 10 hours without producing inflammation; hence they are to be preferred to the resin anhydrids in chronic constipation, or when a strong irritant action is contraindicated.

The seat of action is mainly in the large intestine, and defecation is usually attended with some colic pain, but the small intestine is also affected, though little or no increase in intestinal secretion occurs.

The delayed action is due to the fact that one or more compounds which cause the increased peristalsis are slowly split off from the anthracene nucleus in the alkaline contents of the intestine. Many of these appear to be inactive in the absence of bile, which probably acts merely as a solvent; hence that substance or glycerin and soap are often added to the members of this group.

Numerous synthetic derivatives of anthracene have been proposed, but they are not so useful as the official drugs and as yet have not come into general use.

ALOE.—U. S. P.—Aloes, including the Barbadoes, Curaçao, and the Socotrine, is the inspissated juice obtained from the various species of aloe. It was known to the early Egyptians and Romans. One or the other of the various species of aloes is official in every pharmacopeia. Natal aloes is now interesting only from a scientific point of view.

Average dose (of aloes) : 0.25 gm. (4 grains).

ALOE PURIFICATA.—U. S. P.—This was made official in 1860, because of the impurities present in Socotrine aloes, due to the crude method of collection. The dose is the same as that of aloes.

ALOINUM.—U. S. P.—This is a neutral principle, varying in physical and chemical properties with the variety of aloes from which it is obtained. It does not fully represent the crude drug, medicinally.

Average dose: 0.05 gm. (1 grain).

EXTRACTUM ALOES.—U. S. P.—This is the aqueous extract evaporated to dryness.

Average dose: 0.12 gm. (2 grains).

PILULÆ ALOES.—U. S. P.—Each pill contains 0.13 gm. (2 grains) of purified aloes and an equal amount of soap.

Average dose: 2 pills.

PILULÆ LAXATIVÆ COMPOSITÆ.—U. S. P.—Each pill contains: Aloin, 0.013 gm. (1/5 grain); strychnin, 0.0005 gm. (1/125 grain); extract of belladonna, 0.008 gm. (1/8 grain); ipecac, 0.004 gm. (1/16 grain); and glycyrrhiza, 0.045 gm. (2/3 grain). This is a substitute for the proprietary pills, which under a variety of names have attained a wide popularity.

Average dose (laxative): 1 pill.

The other official preparations into which aloes enters are: Pills of Aloes and Iron, Pills of Aloes and Mastic (the well-known Lady Webster's Dinner Pill), Pills of Aloes and Myrrh, Compound Pills of Rhubarb, Vegetable Cathartic Pills (no calomel), Compound Cathartic Pills, Tincture of Aloes, Tincture of Aloes and Myrrh, and Compound Tincture of Benzoin. The last-named preparation does not contain enough aloes to make it useful as a laxative.

SENNA.—U. S. P.—The Alexandria (short) and the Tinnivelly, or Indian (long), senna are

included in the official title. One, or both, of these is official in every pharmacopeia.

Average dose: 4 gm. (60 grains).

FLUIDEXTRACTUM SENNÆ.—U. S. P.—This is now directed to be made by first removing the resin with strong alcohol and subsequently extracting the drug with diluted alcohol.

Average dose: 2 c.c. (30 minims).

SYRUPUS SENNÆ.—U. S. P.—Syrup of Senna is now a very much more acceptable preparation than was that of the previous Pharmacopeia, and the physician should see that his patient gets the better article when it is prescribed.

It represents 25 per cent. of the fluidextract—from which the principle that causes griping has been removed with alcohol—with oil of coriander to flavor. It supplies an excellent substitute for the nostrums which depend on senna for their activities, such as castoria and the various "fig syrups," so called.

For children one or two teaspoonfuls given alone at bedtime act as a gentle laxative; twice as much may be given as a cathartic. For adults twice as much is given as to children.

This preparation is not disagreeable to the taste, but, since children are usually averse to anything called medicine, it may be given in a little cocoa.

Average dose (as laxative for children): 4 c.c. (1 fluidram).

PULVIS GLYCYRRHIZÆ COMPOSITUS.—U. S. P.—This powder, previously mentioned, contains 18 per cent. of senna. It is widely used as a laxative.

CONFECTIO SENNÆ.—U. S. P.—This represents 10 per cent. of senna, with cassia fistula, tamarind,

prune and fig. It is substantially the same as the well-known proprietary medicine "Tamar-Indien."

Average dose: 4 gm. (60 grains).

INFUSUM SENNÆ COMPOSITUM.—U. S. P.—Formerly known as "black draught" (not black drop). This represents 6 per cent. of senna, and 12 per cent., each, of manna and magnesium sulphate, flavored with oil of fennel.

Average dose: 100 to 200 c.c. (3 to 6 fluid ounces).

The only other official preparation containing senna is: The compound syrup of sarsaparilla, which is useful only as a vehicle.

RHEUM.—U. S. P.—Rhubarb is obtained in Thibet and China from sources still undetermined. This valuable drug has probably been in use longer than any other substance now used wholly as a medicine.

Average dose: 1 gm. (15 grains).

The official preparations of Rhubarb are so numerous that we shall merely enumerate them, most of them being too well known to require extended notice. They are: The Extract, Fluid-extract, Compound Pills, Compound Powder, Syrup, Aromatic Syrup, Tincture and Aromatic Tincture.

The average dose of either syrup is 8 c.c. (2 fluidrams); of the tincture, 4 c.c. (1 fluidram); of the aromatic tincture, 2 c.c. (30 minims).

RHAMNUS PURSHIANA.—U. S. P.—Cascara Sagrada, or "sacred bark," is directed to be gathered a year before being used. It was introduced into

medical practice in 1877, but as a domestic remedy in habitual constipation it was in use some time before that date in the region to which it is indigenous—the Pacific slope. It is now official in a number of pharmacopeias. It is not given in substance.

FLUIDEXTRACTUM RHAMNI PURSHIANÆ.—U. S. P.—This is prepared with 40 per cent. alcohol.

Average dose: 1 c.c. (15 minims).

FLUIDEXTRACTUM RHAMNI PURSHIANÆ AROMATICUM.—U. S. P.—The crude drug contains a bitter acid principle which is neutralized in this preparation with magnesia, orange and glycyrrhiza being added to flavor and sweeten it. There is no special skill required in making this preparation, and any reputable pharmacist can make it equally as well as the manufacturers who put it on the market in the form of proprietary preparations.

Average dose: 1 c.c. (15 minims).

EXTRACTUM RHAMNI PURSHIANÆ.—U. S. P.

Average dose: 0.25 gm. (4 grains).

Pills of aloes afford a convenient form of administration, the soap furnishing the alkali needed for developing the activity of aloes. The pill acts slowly and causes considerable pelvic congestion; hence it is useful in inducing delayed menstruation and increasing it if scanty. For the same reason it, more particularly than other members of the group, is contraindicated in fevers, pregnancy and in inflammatory conditions of the pelvic organs. Alone, it is not so useful in chronic constipation, but it is often added to other purgatives. The compound cathartic pill is the most popular of these combinations.

Bile appears to increase the activity of aloes, and the formula given below is suggestive as a suitable form of administration:

℞. Aloes
Fel. bovis insp.
Saponis .....āā, gr. xx 1|3
M. Ft. pil. No. 15.
Sig.: Three at a dose.

These may be coated with salol, to prevent their disintegration in the stomach. The coating is readily done by simply melting the salol in a shallow tin vessel, into which the pills are then dropped, and the vessel twirled until the salol solidifies. This method of coating is also applicable to other so-called enteric pills, which are intended to dissolve only in the intestine.

The tincture of aloes is so bitter that it is rarely used internally, but it is sometimes applied to bed sores and other local affections. Aloin alone is not so effective as aloes, but it is extremely popular in such combinations as the compound laxative pill, which acts mildly after about sixteen hours.

Senna is one of the best of remedies for chronic constipation, as its use does not entail a still greater tendency to that condition. It has the disadvantage of a disagreeable taste and of causing griping, if used alone; this tendency is overcome by combining it with aromatics. The confection is useful for children and in pregnancy. The milk of the nursing mother who takes senna may purge the child. The resin which causes griping may be removed by extracting the leaves with alcohol without serious loss of the cathartic principle, the offi-

cial fluidextract being made from senna which has been thus treated.

The compound infusion or the confection may be used alone. The compound powder of glycyrrhiza is an extremely popular laxative.

Rhubarb is useful in constipation associated with indigestion and catarrh of the small intestine, but not in chronic constipation, as the tannin present tends to increase the trouble after a time. All of the preparations are useful, but the aromatic syrup and the compound powder are probably the most popular, being especially useful in the summer diarrhea of children. The extract, the fluidextract and rhubarb in powder are all useful laxatives. The compound pills are said to be more useful in the expulsion of gas and in chronic constipation. They are commonly given alone. The following has been much used, but it is largely empirical:

℞. Extr. rhei		
Ferri reducti, āā.....gr. lx	4	
Arseni trioxidi		
Strychninæ sulph., āā.....gr. i		06
Quininæ sulph.....gr. lx	4	

To be made into 40 pills; one to be taken before each meal.

Cascara sagrada is probably the most useful laxative in the materia medica for chronic constipation. Unlike most of these remedies, which demand increasing doses, it improves the digestion, and the dose may be gradually diminished. Owing to the very disagreeable taste of the fluid extract, the aromatic fluid extract, or the extract, in pills or capsules, is to be preferred.

THE ANHYDRID GROUP.

The active principles in drugs of this group are resinous in character; their chemistry is obscure, but most of them are known to be glucosids. They cause violent irritation and even death in excessive doses and are not commonly used alone as cathartics. Since they produce very watery stools, they are sometimes used in dropsy, or to sweep away parasites—for instance, after a narcotic tenifuge, such as aspidium.

The drastics in small doses stimulate peristalsis, and in large doses give rise to inflammatory conditions of the intestine, with serous or bloody diarrhea.

They seem to be inactive in the absence of bile, which acts as a solvent for them as in the case of the members of the anthracene group. They induce increased peristalsis of the small intestine particularly, and evacuation is not usually attended with colic pains except in the case of colocynth, which appears to resemble the members of the anthracene group in its mode of action. Though it, too, causes increased intestinal secretion.

Purgation is usually induced in from 1 to 3 hours.

JALAPA.—U. S. P.—Jalap, the dried tuberous root of *Exogonium purga,* gathered in the neighborhood of Jalapa, Mexico, whence its name. The drug was introduced into Europe about 1609; it is now official in all pharmacopeias. The drug should contain not less than 8 per cent. of total resin,

but not more than 1.5 per cent. of resin soluble in ether.

Average dose (in powder): 1 gm. (15 grains).

PULVIS JALAPÆ COMPOSITUS.—U. S. P.—This is a mixture of 35 parts of jalap and 65 parts of potassium bitartrate.

Average dose: 2 gm. (30 grains).

RESINA JALAPÆ.—U. S. P.—That part of the alcoholic extract which is insoluble in hot water.

Average dose: 0.12 gm. (2 grains).

COLOCYNTHIS.—U. S. P.—The peeled dried fruit of *Citrullus Colocynthis,* a species of cucumber. As "Kolokynthis," this drug was described by Dioscorides and appears to have been well known even before his time; since then it has been in constant use.

Average dose: 0.05 gm. (50 mg. or 1 grain).

EXTRACTUM COLOCYNTHIDIS.—U. S. P.

Average dose: 0.030 gm. (30 mg. or ½ grain).

EXTRACTUM COLOCYNTHIDIS COMPOSITUM.—U. S. P.—Compound Extract of Colocynth is a mixture of 16 parts of extract of colocynth, 50 parts of purified aloes, 6 parts of cardamom, 14 parts of resin of scammony, and 14 parts of soap.

Average dose: 0.50 gm. (7½ grains).

PILULÆ CATHARTICÆ COMPOSITÆ.—U. S. P.—Compound Cathartic Pills. Each contains:

Comp. ext. of colocynth.....gr. iss	08
Mild mercurous chlorid.....gr. i	06
Resin of jalap.....gr. ⅓	02
Gamboge .....gr. ¼	015

Average Dose: 2 pills.

PILULÆ CATHARTICÆ VEGETABILES.—U. S. P.—Vegetable cathartic pills. Each contains:

Comp. ext. of colocynth .....gr. i	|06
Ext. of hyoscyamus .....gr. ss	|03
Resin of jalap .....gr. ⅓	|02
Ext. of leptandra	|
Resin of podophyllum, āā....gr. ¼	|015
Oil of peppermint .....m. ⅛	|008

Average Dose: 2 pills.

SCAMMONIUM.—U. S. P.—Scammony, a gum-resin obtained by incising the living roots of *Convolvulus Scammonia,* has been known and properly esteemed as an active cathartic for over 20 centuries.

Average dose: 0.25 gm. (4 grains).

RESINA SCAMMONII.—U. S. P.—Resin of Scammony is that portion of the gum-resin that is soluble in alcohol, but insoluble in water.

Average dose: 0.2 gm. (3 grains).

PODOPHYLLUM.—U. S. P.—Podophyllum, popularly known as mandrake root or May apple, is said to have been used by the American Indians, but the statement has been repeatedly questioned.

Average dose: 0.5 gm. (7½ grains).

FLUIDEXTRACTUM PODOPHYLLI.—U. S. P.

Average dose: 0.5 c.c. (8 minims).

RESINA PODOPHYLLI.—U. S. P.

Average dose (purgative): 0.015 gm. (15 mg. or ¼ grain); (laxative): 0.005 gm. (5 mg. or 1/10 grain).

LEPTANDRA.—U. S. P.—Is rarely used in substance.

EXTRACTUM LEPTANDRÆ.—U. S. P.

Average dose: 0.25 gm. (4 grains).

FLUIDEXTRACTUM LEPTANDRÆ.—U. S. P.

Average dose: 1 c.c. (15 minims).

[illegible]

[illegible]

[illegible]

Resin of jalap is nearly tasteless and is, therefore, often given to children; it may be mixed with a little sugar for the purpose.

Compound cathartic pills are so well known that they scarcely require further notice. The soap present (in compound extract of colocynth) slowly reduces the mercurous chlorid to the black oxid—increasing its effectiveness.

Podophyllum has been called "vegetable calomel" and it was supposed to increase the secretion of bile, but this is not probable. It causes purgation after ten to twelve hours and is very useful in acute constipation.

A suitable form of administration is suggested below, but the possible combinations are endless. The Triplex Pills (N. F.) have the following formula:

Purified aloes	**gr. ii**	**12**
Mass of mercury	**gr. i**	**06**
Resin of podophyllum	**gr. ¼**	**015**

Dr. John W. Francis has used a pill containing about 1 grain, each, of purified aloes, scammony and mass of mercury, with 1/20 minim of croton oil, ¼ minim of oil of caraway and enough tincture of aloes and myrrh to make one pill.

Leptandra, euonymus and some other official vegetable drugs cause purgation, but do not require special mention here.

PURGATIVE OILS.

There are but two of these which merit discussion here. Castor oil and croton oil owe their activities to two acids, ricinoleic in the castor oil, and crotonoleic in the croton oil. The acid does not exist uncombined in castor oil, but is liberated

when it reaches the intestine, forming new compounds which are irritant and, therefore, purgative.

Crotonoleic acid does exist free to a small extent in croton oil, which is, therefore, irritant even when applied to the skin.

Other bland fixed oils are sometimes used as laxatives. Among those which are official are Olive Oil, Cotton Seed Oil, and Expressed Oil of Almond.

OLEUM RICINI.—U. S. P.—Castor Oil, expressed from the seed of *Ricinus communis*, is a pale, yellowish or almost colorless, transparent, viscid liquid, having a faint mild odor, but an offensive taste. It was known to the ancients, but fell into disuse; it was again brought into notice in 1764 by a West Indian physician, who described it as a gentle purgative.

Average dose: 15 c.c. (4 fluidrams).

OLEUM TIGLII.—U. S. P.—Croton Oil. A pale, brownish-yellow, fixed oil, expressed from the seeds of *Croton Tiglium*; it has a slight fatty odor, and a mild, oily, afterward acrid and burning taste. (Great caution is necessary in tasting.)

Average dose: 0.05 c.c. (1 minim).

Castor oil is very useful in ordinary constipation, and often in diarrhea, when it serves to remove the irritating substance.

Owing to the widespread repugnance to the taste of castor oil, many means have been devised for disguising it. If the mouth is merely rinsed with strong whisky, the oil may be swallowed without discomfort. For children it is given in the form of soda water with syrup of sarsaparilla, or with

ginger ale, when it is often swallowed without the child's knowledge.

The following formula is useful for disguising the taste:

℞. Spts. menth. pip.....ʒiiss 10|
Ol. ricini q. s. ad.....℥iii 100|

Sig.: 15 c.c. (4 fluidrams) to be taken without further dilution.

Emulsions of castor oil have never been popular, as they but imperfectly disguise the taste. Soft capsules, containing 15 minims each, may be swallowed, and many persons find them unobjectionable. Three or four capsules are given at bedtime.

Owing to its irritant character and the violence of its action, croton oil is not generally used as a purgative, but there are conditions in which it is very useful; it may be given in apoplexy, when the patient is unconscious, a drop being placed on the tongue either in the form of an emulsion or on sugar. It is useful when, from any cause, there is difficulty in administering a bulky cathartic, but it is contraindicated in inflammatory conditions of the intestines.

Croton oil is sometimes applied to the skin as an irritant.

LAXATIVE SWEET SUBSTANCES.

Some of the following substances may be treated under the subject of dietetics, since they are laxative mainly because of the bulk of non-absorbable matter. The dose is large and the action mild—with the exception of Cassia Fistula, which is apt to cause griping:

MANNA.—U. S. P.—The concrete saccharine exudation of *Fraxinus ornus.* It consists mainly of a peculiar sugar, mannite.

Average dose: 16 gm. (240 grains).

PRUNUM.—U. S. P.—Prune, the partly dried fruit.

TAMARINDUS.—U. S. P.—The prepared pulp of the fruit.

Average dose: 15 gm. (½ ounce).

FICUS.—U. S. P.—The partially dried fruit.

CASSIA FISTULA.—U. S. P.—The dried fruit. This and the three preceding articles enter into confection of senna.

SALINE CATHARTICS.

The saline cathartics include the slightly absorbable sulphates of sodium and magnesium, and certain of the phosphates, tartrates and citrates. It will be convenient to discuss certain other laxatives, not usually classed as salines, under this heading.

The cathartic salines are those which are slowly absorbed and, therefore, traverse the intestinal canal while containing a considerable amount of water, whereby the feces are kept soft and liquid.

The salines have only a minor direct influence on peristalsis, but they increase it indirectly by means of the increased fluid which they retain.

When concentrated solutions are given, they absorb water until their concentration is equal to that of the blood serum; when dilute solutions are given water is more rapidly absorbed until the same degree of concentration is obtained, and then the solution is absorbed.

Water and alkaline solutions leave the stomach rapidly in the absence of digestive activity and salines are given, preferably, before breakfast, as they then cause little or no nausea and are active in small amounts.

If a concentrated solution is given during digestion it passes slowly into the intestine, and moderate doses may be absorbed without causing purgation.

Failure to purge may follow the use of concentrated solutions after a diet embracing only a small amount of water, as the blood is then more concentrated and the saline solution is incapable of further concentrating it by the additional withdrawal of liquid; on the other hand, the saline is absorbed and is excreted by the kidneys, causing diuresis.

As a certain amount of the saline is always absorbed (often as high as 50 per cent. of sodium sulphate, much less of magnesium sulphate), diuresis very frequently follows, especially after sodium sulphate. The amount absorbed is quite variable, depending on the concentration of the solution, absorbability of the salt and other factors.

As a general routine it is better to administer the saline in fairly dilute solutions, as this spares the work of secretion necessary for diluting them in the stomach and intestine.

Magnesium sulphate is converted into the insoluble carbonate, at least in part, in the intestine, the other salines are excreted unchanged.

The purgative salts, in contrast to the antiquity of many of the vegetable cathartics, are of but

comparatively modern use, many of the inorganic salts being introduced into Europe by the Moors, but not coming into general use until after the time of Paracelsus.

Most of the purgative salts have a disagreeable, bitter taste, but when taken in an effervescing draught this bitterness is masked, and the effervescent salts have, therefore, come into great popularity. The widespread use of nostrums of this type, instead of the official effervescent salts prepared by the pharmacist, illustrates an unfortunate condition which exists without a sufficient reason. There is too much distrust of the pharmacist by certain physicians, who complain that pharmacists are unable to supply preparations equal to those of the nostrum maker. This may possibly be true in isolated cases, but the proof to the contrary is furnished by the extreme simplicity of the preparation of the effervescent salts which the average pharmacist can prepare quite as well as the large manufacturer. Nevertheless the nostrums of this class have an enormous sale.

It is unfortunately true that the physician often lacks confidence in himself and prefers to use the ready-made mixtures rather than to exercise his own choice. This is degrading alike to medicine and to pharmacy.

It is a part of our present purpose to illustrate the ease with which the physician may choose his own agents in the proportion which seems best adapted to each individual case, with the assurance that any honest pharmacist can compound his prescription in a form equal in efficiency and elegance to the nostrums.

The preparation of the effervescent salts depends on the fact that tartaric and citric acids and sodium bicarbonate may be kept in contact without change when dry, but unite with effervescence when they are dissolved in water.

When we see how simple is the preparation of the various effervescent salts, and remember that the Pharmacopeia provides reasonably high standards and readily applied tests for the purity of all official salts, with which all reputable manufacturers of chemicals comply, we see how absurd is the pretense of the nostrum makers that they have special processes and peculiar facilities for manufacturing products of superior quality.

As an example of the ease with which effervescent salts are prepared, we give directions for making one, which, though extremely simple, is still the most complex of those which are official—The Effervescent Magnesium Sulphate. The same directions, with slight modifications, are used in preparing the other official granular effervescent salts and may be used when it is desired to include other salts or even caffein and similar substances.

The magnesium sulphate is dried over a water bath, powdered and mixed with powdered citric and tartaric acids, then with the sodium bicarbonate; the mixture is heated to about 95° C. in a dish placed in an oven until it becomes moist; it is then rubbed through an ordinary tinned iron sieve (which forms it into granules). These are then dried at a temperature of 54° C.

Does it seem credible that any pharmacist is unable to make so simple a preparation as that?

Many of the nostrums that are offered to physi-

cians as effervescent saline mixtures are not even granulated, and some of them, at least, depend entirely on the use of the cheaper *tartaric* acid and sodium bicarbonate to produce effervescence. Mixtures of this kind can be prepared extemporaneously quite as readily as the frequently prescribed liquid preparations.

Constipation is by far the most common complaint of those who live in cities. While the rational treatment consists in attention to the diet and other hygienic measures, for the most part, it is so much easier to read one of the innumerable advertisements which depict the terrible consequences of constipation, and the one certain means of escape therefrom, that the credulous are all too frequently inclined to accept such statements as true.

Any attempt merely to enumerate the nostrums of this type involves one in immediate difficulties, because of the enormous number of those advertised to the public, while those of this type advertised to physicians are scarcely less numerous.

The principal purgative salts and their indications are so well known that we shall confine ourselves mainly to enumerating some of them, with suggestions for the forms in which they are available, and a few of the combinations which may be found useful. We shall have occasion to contrast the well-known actions of these drugs with the absurd claims made for some of the nostrums which they compose.

MAGNESII SULPHAS.—U. S. P.—Epsom Salt (by which name it is most widely known) is so called because it was formerly obtained by evapor-

ating the water of Epsom Springs. It is one of the chief constituents in many famous purgative waters, such, for instance, as the Hunyadi of Hungary.

Average dose: 15 gm. (4 drams).

MAGNESII SULPHAS EFFERVESCENS.—U. S. P. —(Its preparation has been detailed.)

Average dose: 15 gm. (4 drams).

MAGNESII CARBONAS.—U. S. P.—A bulky, white, colorless and nearly tasteless powder, which is insoluble in ordinary solvents.

Average dose: 3 gm. (45 grains).

MAGNESII OXIDUM.—U. S. P.—This, commonly called magnesia, or calcined magnesia, closely resembles the carbonate in its several properties.

Average dose: 2 gm. (30 grains).

MAGNESII OXIDUM PONDEROSUM.—U. S. P.—This differs from the preceding only in being more dense, and therefore requiring a less bulky dose. It was formerly known as Husband's, also as Henry's, magnesia.

Average dose: 2 gm. (30 grains).

LIQUOR MAGNESSI CITRATIS.—U. S. P.—This, almost always called "citrate of magnesia," is one of the most agreeable of the purgative preparations, but it does not keep well, and the freshly prepared solution should therefore be ordered.

Average dose (as purgative): 360 c.c. (one bottle).

Magnesium carbonate is frequently employed as an ant-acid; the oxids, light and heavy, are ant-acid and laxative. The oxids should be given with a large excess of water. They are much used for children.

POTASSII ET SODII TARTRAS.—U. S. P.—This is commonly called Rochelle Salt because it was first manufactured in the city of Rochelle. It was discovered by a pharmacist named Seignette and is often called Seignette salt by the French.

Average dose: 8 gm. (120 grains).

PULVIS EFFERVESCENS COMPOSITUS.—U. S. P. —Seidlitz powder is the form in which Rochelle salt is most often used.

SODII PHOSPHAS.—U. S. P.—This has come into very general use of late years in the treatment of chronic constipation, and it is popularly believed to exert a special influence on the liver. It is soluble in about six parts of water.

Average dose: 2 gm. (30 grains).

SODII PHOSPHAS EFFERVESCENS.—U. S. P.—This is much more pleasant to take than the ordinary sodium phosphate, of which it contains 20 per cent.

Average dose: 8 gm. (120 grains).

SODII PHOSPHATUS EXSICCATUS.—U. S. P.

Average dose: 1 gm. (15 grains).

A preparation so well known as sodium phosphate requires little therapeutic notice, but we wish to offer some suggestions as to the form in which it is available.

The effervescent salt leaves little to be desired when one wishes to employ it as a laxative, but it is not well adapted for use with hot water.

We give below several examples of its combination. In one of these lithium citrate is used. Of course, these combinations may be endlessly varied, using the dried magnesium sulphate, for instance, instead of the dried sodium phosphate.

Caffein is often used with effervescing salts, and this or other similar substances may be incorporated without materially changing the formulas.

℞.	Lithii citratis	ʒi	4
	Sodii phosph.	ʒviii	30
	Sodii bicarb	ʒx	40
	Acidi tartarici	ʒvi	25

The dose of this is about 4 gm. (60 grains).

For use with hot water the following extemporaneously-prepared mixture is preferable to the official effervescent salt:

℞.	Potassii bitart.	ʒx	40
	Sodii bicarb.	ʒv	20
	Sodii phosph. exsic.	ʒx	40

The dose of this preparation is the same as that of the one preceding it. In case a more alkaline mixture is desired the amount of sodium bicarbonate may be slightly increased and the potassium bitartrate correspondingly decreased.

LIQUOR SODII PHOSPHATIS COMPOSITUS.—U. S. P.—One c.c. represents 1 gram of sodium phosphate.

Average dose: 8 c.c. (2 fluidrams).

To make this solution, the Pharmacopeia directs that 100 gm. of sodium phosphate and 4 gm. of sodium nitrate be triturated together in a mortar with 13 gm. of citric acid until completely liquefied, then sufficient water is to be added to make the product measure 100 c.c.

Although this requires no more skill than the weighing of the salts, the Alta Chemical Company pretends that it thus secures "An Ideal Nerve Tonic, Laxative, Analgesic! Stimulant of Glandular Function, adjuvant to all organic remedies indicated in the organism! relieving Hepatic Con-

gestion, supporting Sexual Power, regulating both excretion and secretion on a normal physiologic basis!"

The indications enumerated need not be re-repeated in full, but as an example of the misrepresentation practiced by this firm we quote the following: "Especially reliable as a painless cure for the Morphin Habit!" Rheumagon, consisting of sodium iodid and sodium phosphate, is "a specific in all cachetic diseases."

Does this insolent company suppose that we are bereft of every vestige of intelligence when it persists in making such statements?

It must be evident to the least observant that we are drifting far from the safe course in therapeutics when men, who have not sufficient knowledge to avoid absurdities so glaring that they become apparent on the first appeal to reason, exploit our profession and use us to dupe the public. Are we to continue in this degrading position or are we to assert our independence and demand common sense, at least, from those who seek to serve us? The arrogance of the nostrum vendors under the cloak of servility is becoming insupportable, and physicians should no longer tolerate such abuses.

MERCURIALS.

Despite the widespread use of the mercurials, their mode of action remains a problem. Some authorities assert that calomel must be controverted into the oxid, others that small amounts of the bichlorid are formed, and that this is the active agent. The effect on the organism is not less a matter of dispute; pharmacologists usually deny

that it causes an increase of bile-flow, as experiments, made by careful observers, on both man and animals with biliary fistula, have failed to demonstrate any increase. Calomel acts as an antiseptic and the bile is thus protected from decomposition, while the increased peristalsis affords less time for its absorption. Some of the older clinicians, however, still hold to the theory that it really does increase the amount of bile secreted by the liver. However calomel may act, it is the best remedy we possess for that form of indigestion and constipation which is frequently called "biliousness."

HYDRARGYRUM CUM CRETA.— U. S. P.—Gray Powder.—This contains 38 per cent. of mercury (metallic) mechanically mixed with clarified honey and prepared chalk.

Average dose: 0.25 gm (4 grains).

MASSA HYDRARGYRI.—U. S. P.—The well-known "blue mass" contains 33 per cent. of mercury (metallic) combined with glycyrrhiza, althea, glycerin, and honey of rose.

Average dose: 0.25 gm. (4 grains).

HYDRARGYRI CHLORIDUM MITE.—U. S. P.—Calomel is required by the Pharmacopeia to contain at least 99.5 per cent. of pure mercurous chlorid.

There is, perhaps, no drug which is better known than calomel, and we can afford to give it space in inverse proportion to its importance.

Average dose (as a laxative): 0.12 gm. (2 grains).

Mercury and chalk, commonly called gray powder, does not occasion so much nausea as the other

mercurials in common use, and is usually preferred for children who suffer with indigestion and constipation with considerable intestinal putrefaction.

The mercurials are contraindicated in chronic conditions, such as tuberculosis, and in the latter months of pregnancy. The use of calomel as a diuretic has been mentioned, and while Wood pronounces it useful in chronic parenchymatous nephritis, others maintain that it is injurious, and Sollmann has recently suggested that great conservatism should be exercised in its employment. At any rate, it should not be used merely for its purgative effect when nephritis exists, or only with great caution.

SULPHUR PRECIPITATUM.—U. S. P.—SULPHUR SUBLIMATUM.—U. S. P.—and SULPHUR LOTUM. U. S. P.—These are the three forms in which Sulphur is now official. Either the sublimed or the washed may be used as a laxative. The sulphur is slowly converted in the intestine into the sulphid of sodium only to a small extent, which stimulates peristalsis, while the greater part of the sulphur remains insoluble and acts mechanically—merely by its bulk. Washed sulphur is an ingredient of compound powder of glycyrrhiza. Precipitated sulphur is a very fine powder, and consequently it is converted much more quickly into the sulphid of sodium, giving rise to irritation, hence it is not used as a laxative.

Since many of the symptoms resulting from indigestion and constipation were formerly attributed to a deficiency in the formation of bile, agents were sought which would increase its secretion.

Many of the purgatives now in common use were supposed to possess this property, but the only agent which has been shown by experiment to increase the secretion notably is bile itself.

Philip Shaffer recently gave a woman with biliary fistula about 20 gms. (5 drams) of the purified ox bile in three days, resulting in a notable increase of bile secretion.

This can scarcely be considered as a stimulation of the liver to increased production of the bile, for it seems probable that the ingested bile was absorbed and again excreted by the liver. Even though this function of the liver were increased there is no evidence that a corresponding increase in the other functions occurs. In any event the official dose of bile is too insignificant to exert any notable effect on the total amount for the twenty-four hours, since a healthy adult normally secretes about 500 c.c. in that period.

The patient's general condition seemed to be but little affected by the absence of bile from the intestine, but fats were not so well borne as in a normal person. This but confirms the experience of other observers, and in this light cholagogues lose much of their importance.

The precise rôle played by bile beyond the splitting of fats is still a moot point.

In this connection it may be mentioned that the mineral acids, particularly the dilute nitro-hydrochloric, have been much used for their supposed cholagogue action; this is too slight to give them practical value, but they are useful in many conditions for which a deficiency of bile is supposed to be the cause.

FEL BOVIS.—U. S. P.—The fresh bile of the ox is used only in the form of:

FEL BOVIS PURIFICATUM.—U. S. P.—Its use has already been mentioned.

Average dose: 0.5 gm.

ATROPIN.

The action of atropin in the intestine is still a matter of dispute. It is well known that direct applications to the serous surface inhibit reflex peristalsis, but it has been maintained that very small amounts in the lumen increase peristalsis. The seat of action is not known, but presumably it is on the musculature of the intestinal wall. It may be that it tends to lessen local constriction which would interfere with peristalsis; at any rate the addition of small amounts of atropin or, better still, extract of belladonna, to some of the laxatives, as in the compound laxative pills, seems to be distinctly beneficial.

PHENOLPHTHALEIN.

Phenolphthalein is not official as a medicinal substance, but is mentioned in the Pharmacopeia, in the list of reagents and test solutions, as an indicator in acidimetry.

It has attracted some attention of late as a laxative. In combination with soap and salicylic acid it is being widely advertised under the name of "Probilin."[1]

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1. The proprietors of probilin quote Dr. W. Bauermeister of Brunswick, Germany, as authority for the assertion that salicylic acid and sodium oleate are the most powerful cholagogues. This is not in accord with the generally accepted opinion of therapeutists. The same authority states that he had the two drugs put up in pills containing 1½

GLYCERIN.

GLYCERINUM.—U. S. P.—Glycerin, or, as it is more properly designated, glycerol, is frequently used in place of the ordinary form of enema as a rectal injection for the purpose of producing a rapid evacuation of the content of the lower bowel.

For the usual form of glycerin injection from 4 to 15 c.c. (1 to 4 fluidrams) are diluted with an equal portion of water and injected with a rectal syringe.

SUPPOSITORIA GLYCERINI.—U. S. P.—Suppositories of glycerin are generally preferred to other forms of administering glycerin. As now official they contain approximately 3 grams (45 grains) each of glycerin gelatinized by means of a hard soap, made from stearic acid and sodium carbonate.

While there is considerable difference of opinion as to how glycerin acts when used locally in the rectum, it is generally supposed that its action is in part mechanical and in part due to a peristalsis occasioned by the irritation of the mucous membrane of the rectum, produced by the hygro-

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grains of each, adding menthol and phenolphthalein as analeptics and to mildly stimulate intestinal activity.

From a chemical examination of probilin pills, made for the Council on Pharmacy and Chemistry of the American Medical Association (*Jour. A. M. A.*, August 24, 1907, page 702), it appears that the true composition of this preparation differs materially from the formula, as published at that time, and is about as follows:

Phenolphthalein, 0.008; sodium salicylate, 0.01; sodium oleate and free oleic acid, 0.10; menthol, 0.01; moisture, 0.006; dusting powder, 0.065.

The dusting powder appears to be made up of lycopodium, licorice and charcoal.

Under date of Oct. 5, 1907, Messrs. Schering and Glatz publish a revised formula for probilin, which practically agrees with the analysis as given above.

scopic properties of the glycerin. Authorities generally agree that while the occasional use of glycerin in the rectum is devoid of harm, that the persistent or the continued use is injurious to the mucous membrane of the rectum.

TREATMENT OF CONSTIPATION.

First in the treatment of constipation, for which purgatives are well-nigh universally employed, stands diet. By this means alone a very large proportion of cases of chronic constipation might be cured. It should contain a certain amount of indigestible residue, contrary to popular belief, and if the patient, in addition to correcting the diet, takes a fair amount of exercise in the open air and goes regularly to stool, but little purgative medicine will be needed. It should be remembered that a glass of cold water, alone, taken on rising, will often act as a laxative.

Such simple remedies should always be tried before resorting to drugs in chronic constipation, since the habit of taking laxatives is easily formed, but not so easily abandoned.

Hydragogue cathartics are sometimes used in dropsy and to afford relief for the kidney.

The excessive development of bacterial poisons in the intestine and their absorption into the blood cause symptoms varying from mere lassitude to profound shock. Purgatives sweep the bacteria and their poisons from the canal.

Diarrhea, due to the presence of irritating matter, such as undigested and fermenting food, is often promptly relieved by a saline purge. Saline purgatives are also useful in reducing fever, but

they are not suited to cases of the asthenic type, because of the exhaustion which they produce.

The preparations of the crude vegetable cathartics are usually but slightly soluble in water and dilute acids, but readily soluble in alkalies; they are, therefore, not absorbed from the stomach to any great extent, but, being soluble in the intestinal contents, they act by irritating the bowel. They are much slower than salines in their action, producing evacuation of the intestine usually only after from five to sixteen hours with moderate doses. These facts are of much importance in choosing a purgative when there is inflammation of the intestine or other abdominal organs, as well as in pregnancy, since the irritation of the more drastic cathartics, by extending to the gravid uterus, may induce premature expulsion of the fetus.

CHAPTER XVIII.

EMMENAGOGUES AND ANTISPASMODICS.

Several groups of agents will be considered in this chapter, since each group scarcely deserves a separate chapter in this book. Not that many pages of medical literature have not been devoted to each subject, but because their importance is such that they should be especially studied in more comprehensive works.

EMMENAGOGUES.

Emmenagogues are agents which stimulate the menstrual flow, if they are given at the menstrual period, and which act as ecbolics or oxytocics when given during pregnancy or at term.

Drugs which are irritant to the gastrointestinal canal, such as aloes and the drastic purgatives, as well as quinin, castor oil and a number of other substances, are often given at term to induce labor. Heat in the form of hip baths and vaginal douches, and counterirritants, such as mustard, are useful as emmenagogues but not as ecbolics.

Various volatile oils and cantharidin are frequently used with criminal intent, but these may cause death without expelling the fetus.

ERGOT.

Ergot is a fungus of very complex, and probably variable, composition which has thus far defied successful analysis. Active principles can be iso-

lated from ergot, in a pure state, only with difficulty or not at all, and the constituents so far examined are not very stable.

Of the numerous substances that have been isolated from ergot there are but three that have received widespread recognition. These are ergotinic acid, cornutin and sphacelotoxin. Even these are probably compounds or mixtures which differ somewhat in their behavior. Since they are generally recognized as representing the activities of ergot their actions may be briefly considered.

Ergotinic acid is a saponin-like substance which is decomposed in the gastrointestinal canal, hence its action is merely local, being an irritant when the drug is given by the mouth. It is depressant to the nervous system when injected into the blood, and as it does not participate in the medicinal action of ergot, preparations of ergot intended for subcutaneous injection should be freed from it.

Cornutin is also, probably, a compound, but is usually spoken of as an alkaloid. Its action is almost exclusively on the medulla, whether the preparation is injected or given by the mouth. The isolated principle causes a rise of blood pressure and increased peristaltic movement of the uterus. Kobert attributes the power to cause gangrene to this substance, and latterly he suggested that it helps to expel the fetus. Large doses of cornutin cause convulsions.

Sphacelotoxin is not stable, but in certain combinations it is fairly so. It causes constriction of the blood vessels and results in gangrene in parts of certain animals, as in the comb and wattles of the rooster. Since this appears to be the active

ecbolic principle of ergot, the action on the rooster's comb and wattles affords an easy method of testing its physiologic activity. Ergot deteriorates very rapidly, and commercial preparations of it are, necessarily, very variable. A good preparation, however, is much more stable than is the drug itself, hence preparations once tested may be depended on for a number of years.

The physiologic test is so simple that any physician may apply it, and the importance of having a reliable preparation is so obvious that we give the method that is ordinarily followed in testing a fluidextract of ergot.

A rooster with a bright red comb and wattles is chosen and 5 c.c. of the fluidextract is injected subcutaneously, or it may be added to crumb of bread, made into a paste and pushed down the craw with the finger. Within an hour or more the tips of the comb and wattles are found to be much cooler than before the injection; the color changes from bright red to dark (venous) and may become black. The rooster may become drowsy and refuse food for a few days. If unsuccessful, the experiment should be repeated on another rooster before condemning the preparation, as some roosters are not susceptible.

It is obvious that when ergot is taken by the stomach the systemic action is due to the cornutin and sphacelotoxin, of which the latter is probably much the more important.

The use of ergot for internal hemorrhage, except from the uterus, is irrational so far as may be judged from pharmacologic experiments. While the results of different investigators of ergot and

its derivatives are far from uniform, many of the discrepancies that have been noted may be explained by differences in the substances used, due either to the method of preparation, natural deterioration of the crude drug or to variations in normal constituents. It must also be remembered that many of the experiments that are recorded were made by injecting the drug into the vein, whereby the action of ergotinic acid is brought out more prominently, which is not the case with subcutaneous or intramuscular injections or oral administration.

There can be little doubt that when ergot is administered, just after the head of the child emerges, its active constituents will be absorbed from the stomach and will tend to lessen the danger from postpartum hemorrhage by causing the uterus to contract firmly.

The value of ergot as an ecbolic has been questioned, and many careful obstetricians advise that it be given only after the expulsion of the placenta, lest the uterus contract firmly upon it and prevent extrusion. If the drug is given before the placenta is expelled, large doses at least must be avoided.

Large doses, given in the early stages of labor, have resulted in tonic contraction and rupture of the uterus. Quinin is a much safer drug to produce strong uterine contractions, since tetanic contraction does not follow its use. The results of different investigators with hydrastinin are contradictory.

Various modifications of the official preparations of ergot have been put on the market, but it seems hardly necessary to reiterate that any of these

should be carefully tested rather than that we should rely too implicitly on the statements of the manufacturers, particularly when these are comparatively unknown to the physician. Some of the more reputable firms now test their fluidextract of ergot before sending it out, and while it must be admitted that this test is qualitative rather than quantitative, it does assure a reasonably safe guide for uniformity.

Ergot and its preparations are official as

ERGOTA.—U. S. P.—The sclerotium of *Claviceps purpurea,* replacing the grain of rye. On account of the variable nature of the drug itself, particularly in the form of powder, it is now seldom used in this form.

Average dose: 2 gms. (30 grains).

EXTRACTUM ERGOTÆ.—U. S. P.—This is really a purified extract and represents eight times its weight of the crude drug. It includes a small proportion of sodium chlorid and about 10 per cent., by weight, of glycerin. A somewhat similar preparation, without the glycerin, is known in England as "ergotin."

Average dose: 0.25 gm. (4 grains).

FLUIDEXTRACTUM ERGOTÆ.—U. S. P.—Fluidextract of ergot is directed to be made with diluted alcohol containing 2 per cent. of acetic acid.

Average dose: 2 c.c. (30 minims).

VINUM ERGOTÆ.—U. S. P.—Wine of ergot, as now official, is a simple dilution of twenty parts of fluidextract of ergot with a sufficient quantity of fortified white wine to make 100 parts.

Average dose: 8 c.c. (2 fluidrams).

Of the many drugs that have been suggested as substitutes for ergot but two need be mentioned.

Corn Smut, Ustilago, was at one time official in this country. Resembling ergot in origin, it was thought to have similar uses; clinical experience, as well as pharmacologic investigations, however, showed that it was sometimes quite inert.

GOSSYPII CORTEX.—U. S. P.—The dried bark of the root of *Gossypium herbaceum* was, formerly at least, asserted to have uses similar to those of ergot. It has been shown to have little or no effect on animals, and more careful clinical observation will probably demonstrate that its further continuance as an official drug is not warranted. A fluid extract, formerly official, has been discontinued.

The treatment of excessive menstruation demands the consideration of the underlying cause. It may be the result of anemia, in which case diet and the use of hematinics will prove useful, or general tonics may be required.

The treatment of hysteria has long depended largely on a number of substances, usually classed as antispasmodics, that differ widely in composition and agree mainly in possessing a disagreeable odor, to which Sollmann attributes their efficiency.

Their pharmacologic action gives no clue to their clinical use, but we must accept clinical experience as having established their value. It is in precisely such conditions, where scientific medicine must often confess itself ignorant, that the charlatan and the nostrum-maker find their greatest opportunities. While it must be considered as extremely improbable that ignorant unscientific men should solve mysteries which have baffled the

most careful observers, even a superficial review of the following list of official substances will reveal them as being the active ingredients in a number of nostrums that have been widely used and are still popular with medical men as well as the laity.

OFFICIAL ANTISPASMODICS.

ASAFŒTIDA.—U. S. P.—This drug has long been popular as a condiment and as a carminative. Its use as an antispasmodic is probably of later origin.

Average dose: 0.25 gm. (4 grains).

The official preparations are: the pill, tincture and emulsion of asafetida, enumerated under stomachics.

SUMBUL. — U. S. P. — This drug, commonly known as musk root, consists of the dried rhizome and root of an undetermined plant, probably of the family *Umbellifera.*

Average dose: 2 gms (30 grains).

Coming from Central Asia, the home of the musk deer, and having an odor somewhat suggestive of musk, this drug was early seized upon by the manufacturers of nostrums as offering good points for commercial exploitation. Apart from its rather unpleasant odor, due to a volatile oil, a resin and a trace of valeric acid, this drug does not appear to offer any particular reasons for its continued popularity.

The official preparations are:

FLUIDEXTRACTUM SUMBUL.—U. S. P.—This is made with a menstruum containing 75 per cent. of alcohol.

Average dose: 2 c.c. (30 minims).

EXTRACTUM SUMBUL.—U. S. P.—This is directed to be made by concentrating the fluidextract.

Average dose: 0.25 gm. (4 grains).

VIBURNUM OPULUS. — U. S. P. — Viburnum Opulus, or cramp bark, is another drug that has been freely exploited by makers of proprietary remedies, by whom ridiculously incongruous properties have been claimed for it. Careful chemical examination, on the part of a number of investigators, shows that it contains a bitter, somewhat resinous, principle and a trace of valeric acid.

Average dose: 2 gms. (30 grains).

The only official preparation is

FLUIDEXTRACTUM VIBURNI OPULI.—U. S. P.—This is directed to be made with a menstruum containing two parts of alcohol and one part of water.

Average dose: 2 c.c. (30 minims).

The National Formulary contains several preparations of a complex nature, neither better nor worse than the numerous, more or less similar trade articles which are so widely advertised in medical as well as lay journals, and which they are designed to replace. One of these, the use of which is not recommended, is

TINCTURA VIBURNI OPULI COMPOSITA.—N. F.—This represents in each average dose (4 c.c. = 1 fluidram) 0.25 gm. (4 grains) each of viburnum opulus and dioscorea (wild yam) with scuttellaria and aromatics.

VIBURNUM PRUNIFOLIUM.—U. S. P.—This is officially described as the dried bark of the root of *Viburnum prunifolium* or of *Viburnum lentago.* This drug has been exploited for the same pur-

poses and in much the same way as viburnum opulus.

Average dose: 2 gms. (30 grains).

FLUIDEXTRACTUM VIBURNI PRUNIFOLII.—U. S. P.—This preparation, like the corresponding preparation of viburnum opulus, is made with a menstruum containing two parts of alcohol and one part of water.

Average dose: 2 c.c. (30 minims).

VALERIANA.—U. S. P.—Valerian, as now official, consists of the dried rhizome and roots of *Valeriana officinalis.* This drug has been in continued use in Northern Europe for several centuries. In England it appears to have been used at one time as a condiment for "physicall broths and meats."

Average dose: 2 gms. (30 grains).

TINCTURA VALERIANÆ.—U. S. P.—This preparation represents 20 per cent. of the crude drug in 75 per cent. alcohol.

Average dose: 4 c.c. (1 fluidram).

TINCTURA VALERIANÆ AMMONIATA.—U. S. P.—The Ammoniated Tincture of Valerian represents 20 per cent. of the crude drug extracted with aromatic spirit of ammonia.

Average dose: 2 c.c. (30 minims).

FLUIDEXTRACTUM VALERIANÆ. — U. S. P. — This is directed to be made with 75 per cent. alcohol.

Average dose: 2 c.c. (30 minims).

ZINCI VALERAS.—U. S. P.—Zinc Valerate occurs as white, pearly scales, having the odor of valeric acid. It is but sparingly soluble in water

or in alcohol and is preferably directed to be given in either pill or capsule.

Average dose: 0.12 gm. (2 grains).

AMMONII VALERAS. — U. S. P. — Ammonium Valerate (or valerianate in former pharmacopeias) occurs as colorless or white, quadrangular plates having the characteristic odor of valeric acid. It is freely soluble in water and in alcohol.

Average dose: 0.50 gm. (7½ grains).

The National Formulary contains several formulas for liquid preparations of ammonium valerate. The most popular of these is

ELIXIR AMMONII VALERIANATIS.—N. F.—The average dose (4 c.c. = 1 fluidram) of this preparation contains about 0.14 gm. (2 grains) of ammonium valerate in aromatic elixir colored red, with tinctura of cudbear.

CHAPTER XIX.

PARASITICIDES AND ANTIGONORRHEICS.

It will be convenient to consider under this head, agents used for parasites other than bacteria, which infest the skin and intestines, together with a brief reference to the antigonorrheics.

Cleanliness prevents nearly all hurtful skin parasitism, and, as the greater number of skin affections are commonly treated more advantageously by the specialist, all that we shall attempt to do is to call attention to several of the different classes of parasites that infest the human skin, and enumerate some of the official remedies that have been used with success in their treatment.

Tinea sycosis, barbers itch, is one of a group of skin diseases due to a vegetable parasite, *tricophyton tonsurans,* which attacks the hair follicles.

Scabies, or itch, is an animal parasitic disease, generally due to the common itch mite, *Sarcoptes scabies,* though there are a number of other species of Acarida that occasionally infest the human skin.

In the treatment of all skin diseases of parasitic origin, cleanliness is a matter of prime importance as a preliminary to the treatment with parasiticides or antiseptics. Among the remedies that have been used for this type of affection we may enumerate:

SAPO MOLLIS.—U. S. P.—The official soft soap is directed to be made by saponifying linseed oil with potassium hydroxid. It is particularly efficient as a detergent and is frequently directed, with hot water, as a preliminary to the treatment of scabies with:

UNGUENTUM SULPHURIS.—U. S. P.—This ointment contains 15 per cent. of washed sulphur in benzoinated lard. Some practitioners prefer:

UNGUENTUM SULPHURIS COMPOSITUM.—N. F. —This is also known as Wilkinson's ointment and as Hebra's itch ointment, and contains precipitated calcium carbonate, 10; sublimed sulphur, 15; oil of cade, 15; soft soap, 30, and lard, 30 parts. It is a fair representative of the composite type of ointment, used for scabies, and may be varied readily to suit the particular indications in any one case.

Sulphur and sulphur-containing compounds are also used for various forms of vegetable parasites. Among the official substances that are used in this way we have:

SODII THIOSULPHAS.—U. S. P., and:

SODII SULPHIS.—U. S. P.

These two substances are readily soluble in water and are usually employed in the form of a lotion containing approximately 10 per cent. of either of the substances in aqueous solution.

Mercurials are also used quite frequently in the treatment of skin affections of parasitic origin. In addition to the soluble salts of mercury, used in the form of lotion, we have the widely used:

UNGUENTUM HYDRARGYRI AMMONIATI.—U. S. P.—This ointment contains 10 per cent. of ammo-

niated mercury in a mixture of white petrolatum and hydrous wool fat.

The louse which infests the head requires no medication, since it is easily removed with a fine comb and thorough washing with tar soap. The ointment of red mercuric oxid or red precipitate has been used as a popular domestic remedy, and the fluidextract of larkspur, or of stavesacre, may be useful in many cases.

The louse, *Pediculus pubis,* which infests the genital regions is smaller and more difficult to remove mechanically.

A dilute solution of mercuric chlorid (corrosive sublimate) is sometimes used and is very effective for this troublesome parasite. It should not be stronger than one to five hundred (2 grains to 2 fluidounces or 0.1 gm. to 50 c.c.), and this should be used cautiouusly. A less cleanly but very efficient remedy is mercurial ointment.

A 20 per cent. tincture of staphisagria, or larkspur, diluted with water, bay rum, dilute alcohol or soap liniment is much used in some parts of the country.

Among the names of staphisagria which indicate its common use are semen staphidis pedicularis and läusekörner.

In lieu of the unofficial tincture the now official:

FLUIDEXTRACTUM STAPHISAGRIÆ.—U. S. P.—Diluted with from 8 to 10 parts of soap liniment, or of bay rum, will be found equally serviceable.

It may be prescribed as follows:

℞.	Hydrarg. chlor. cor.	gr.i	05
	Fluidext. staphysagriæ	fl℥i	5
	Alcohol	fl℥i	30
	Aquæ rosæ, q. s. ad	fl℥iii	100

Misce.

Sig.: Apply as a wash.

This will be found to be effective and, of course, much more cleanly than the mercurial ointment which is very commonly used.

It may not be amiss to call attention to the fact that carbolic ointment not only kills the troublesome chigger, but also relieves the smarting which that parasite occasions, or which is more frequently caused by scratching the place where the parasite is embedded.

ANTHELMINTICS.

The term anthelmintic, meaning literally against a worm, embraces vermifuges and teniafuges, which expel the round or tape worms, respectively, and vermicides and tenicides which kill them; but, as a matter of fact, the parasites are rarely killed before their expulsion.

Küchenmeister attempted to establish a rational basis for the use of anthelmintics, more than fifty years ago, but his work, which was widely quoted for a long time, has but little value at present.

The effects of a large number of vermifuges were studied by von Schroeder, who found that ascarides are remarkably resistant to poison placed in the media with the parasites, which are to a certain extent able to resist absorption. These parasites are surrounded by a chitinous substance, and when that is not acted on by the agent the mouth is the principal means of ingress to their bodies. Santonin, even in concentrated solution,

was found to be harmless to the parasite, which, however, found it objectionable and sought to escape from the solution containing it, the movements being particularly active; from this it would appear that santonin drives the round worm out of its normal habitat into the large intestine, from which it must be swept by purgation.

Santonin is insoluble in neutral and acid media, hence it is not absorbed from the stomach, but it appears to be in part converted in the intestine into the sodium santoninate, which is soluble, and which undergoes absorption. This may give rise to such symptoms of poisoning as convulsions, vomiting and diarrhea.

If any of the poison still remains in the stomach when toxic symptoms are observed, it should be evacuated, and rapidly acting purgatives, such as castor oil and the salines, may be used to hasten the elimination from the intestine. Purgatives of the anthracene group act too slowly, and drastics are too depressant to be useful in such cases. Santonin is excreted in the urine; hence a rapidly acting diuretic, such as hot tea, may be of service. The urine is colored yellow (red if alkaline) after ordinary doses of santonin.

Small doses of santonin give rise to what is commonly termed yellow vision; this is due to some peripheral action whereby white light appears violet, then yellowish, but the media of the eye is not discolored.

The statement that the presence of castor oil greatly increased the toxicity of santonin for worms arose from a mistake, and santonin is now usually given with calomel. Since it is not

intended to be dissolved in the stomach, a compressed tablet or lozenge of calomel and santonin is to be preferred. For the same reason, when santonin is given to a child, with a little sugar, the two substances should be lightly rubbed together without being powdered. Sodium santoninate, which is soluble, should not be used, therefore, and very properly, it has been dismissed from the later editions of our Pharmacopeia.

The following are among the now official substances that are useful as vermifuges:

SANTONICA.—U. S. P.—Santonica or Levant worm seed, as it is frequently called, is officially described as the dried unexpanded flower heads of *Artemisia pauciflora*. It is now seldom employed as such, being generally displaced by:

SANTONINUM.—U. S. P.—Santonin, the inner anhydride or lactone of santonic acid, obtained from santonica, was discovered in 1830, by two German apothecaries, quite independently of each other, Kahler in Düsseldorf, and Alms in Mecklenburg.

Average dose: 0.06 gm. (1 grain).

SPIGELIA.—U. S. P.—Spigelia or pink root is the dried rhizome and roots of *Spigelia marilandica.*

Average dose: 4 gm. (60 grains).

FLUIDEXTRACTUM SPIGELIÆ.—U. S. P.—This is made with diluted alcohol and is the preparation now generally used when this drug is to be administered.

Average dose: 4 c.c. (1 fluidram).

OLEUM CHENOPODII.—U. S. P.—Oil of Chenopodium is a volatile oil distilled from *Chenopo-*

dium anthelminticum, more popularly known as American wormseed.

Average dose: 0.2 c.c. (3 minims).

QUASSIA.—U. S. P.—The wood of *Picrasma excelsa,* Jamaica quassia, or of *Quassia amara,* Surinam quassia, is more frequently used in the form of a decoction or an infusion, made in accordance with the general formulas for these several preparations.

Average dose: 0.5 gm. (7½ grains).

EXTRACTUM QUASSIÆ.—U. S. P.—This is an aqueous extract and represents ten times the weight of the crude drug.

Average dose: 0.06 gm. (1 grain).

FLUIDEXTRACTUM QUASSIÆ.—U. S. P.—This is directed to be made with a mixture of three parts of alcohol and six parts of water.

Average dose: 0.5 c.c. (8 minims).

TINCTURA QUASSIÆ.—U. S. P.—This is a 20 per cent. tincture and is made with 35 per cent. alcohol.

Average dose: 2 c.c. (30 minims).

The *Ascaris lumbricoides,* or round worm, is a very common parasite in the small intestine of children particularly. The most useful remedy for this parasite is santonin; this has been given in a variety of methods. Some authorities recommend from one-half to one grain (0.02 to 0.05 gm.) morning and evening during three days for a child and on the fourth day a purgative. This suggestion was evidently based on the supposition that the parasites were killed or injured and were then to be swept out, but since we know that this is not true, the method in vogue at the present

time is to combine santonin with a slowly acting purgative, such as calomel in small doses. The purgative should follow the santonin in a few hours at the latest. It should be remembered at all times that santonin is not an absolutely safe remedy and that it is far better to try a small dose and to repeat it in a few days if not effective than to give the maximum dose in the beginning.

A lozenge containing half a grain (0.03 gm.) of santonin given morning and evening, to a child, for three days will usually be found effective. Twice this dose is used for an adult.

If it is desired to give santonin in powders, it may be prescribed somewhat as follows:

℞. Santonini (cryst.) .....grs. iii 0|2
Sacchari .....grs. xxx 2|
M. Ft. in chart, No. vi div.
Sig.: One powder night and morning, the last dose to be followed by a purgative.

The purgative may consist of calomel or syrup of senna, or, according to the more modern teaching, 1/6 grain (0.01 gm.) of calomel may be directed to be incorporated in each paper. The mixture should be dispensed in granular form and not finely powdered. Santonin taken in this way has very little taste.

While santonin is perhaps the most effective remedy we have for ascarides, the fluidextract of spigelia has been recommended and is said to act somewhat like santonin. It is recommended that a laxative be given before the spigelia and a purgative some hours later, or the combination of pink root and senna, that was at one time quite common, may be preferred.

Spigelia, however, has also given rise to toxic symptoms in children.

Oil of chenopodium, or oil of American wormseed, has long enjoyed a certain reputation, particularly as a household remedy, for round worms. It has a very disagreeable odor and taste. It may be given combined with castor oil, or from one to three drops may be mixed with sugar for a child.

The thread worm or pin worm, *Oxyuris vermicularis,* infests the rectum and colon, and is often spoken of as the seat worm.

The common anthelmintics, such as santonin, together with purgatives, are usually effective in removing them, but they sometimes prove very troublesome and difficult to dislodge.

Injections of large amounts of watery infusions are often useful. Infusion of quassia enjoys an especial reputation, it lessens the mucus secretion and probably increases the movements of the parasites, which facilitates their removal when the bowel is emptied.

As suggested in connection with the official preparations of quassia, an aqueous infusion, the extract or even a correspondingly diluted fluidextract may be used, with some promise of satisfactory results, in cases in which the infusion can not be readily obtained.

Phenol has also been recommended, but the danger of absorption entirely precludes its common use.

Thymol is sometimes used for a parasite which infests the duodenum, *Anchylostomum duodenale,* not uncommon in Italy, but not often seen in this country.

Osler recommends the cold injection of a strong solution of common salt for children, repeated for ten days at least. The hips are elevated to favor the retention of the injection as long as possible.

TENIAFUGES.

Remedies used for tape worm are commonly spoken of as teniafuges, even though the parasite may belong to a genus other than Tænia, but, as a matter of fact, the *Tænia saginata,* which is derived from beef, is very much more commonly found in the human intestine, while *Tænia solium* from swine is met with much less frequently in man, and *Bothriocephalus latus,* though mentioned in all text-books, is extremely rare in this country and practically never originates here, hence it may be disregarded in this place.

It should be remembered that the various agents used as teniafuges are not free from danger and should not be used until a diagnosis has been positively made by the appearance in the feces of parts of the parasites or the eggs.

Male fern, or the much more widely used oleoresin, which fully represents the rhizome, is said to be very much less efficacious against the *Tænia* than against the *Bothriocephalus,* while pelletierin, obtained from the bark of pomegranate root, is especially efficacious against the *Tænia.* If this be true we have but another example of our tendency to take everything originating in Germany as being universally applicable, without exercising our own judgment, for male fern has certainly enjoyed a greater popularity than the circumstances appear to justify. On the other hand, its wide use in

northern Germany is more rational, since the *Bothriocephalus* is very commonly found there in man.

It was found by von Schroeder that one part of pelletierin in ten thousand parts of a solution containing 1 per cent. each of sodium chlorid and sodium carbonate, was very rapidly fatal to *Tænia serrata* and to *Tænia inermis,* while much stronger solutions were practically harmless to round worms.

Estimating the content of the human intestine at 200 c.c. after purgation, if only 0.2 gm. (3 grains) of pelletierin escape absorption from the stomach and pass into the intestine, it would be present in the proportion of one part in one thousand of intestinal content, or ten times the concentration found necessary by von Schroeder.

Pelletierin is but mildly toxic to man; hence it appears to be an almost ideal teniafuge or tenicide.

Kamala, which was formerly official, and is still used, acts as an intestinal irritant, causing purging and, therefore, requiring no subsequent purgative. It is said to be effective against tenia and is usually administered in substance, being given in doses of from 4 to 8 gm. (one to two drams).

Kosotoxin, obtained from kousso, resembles male fern in its pharmacologic action, but is said to be efficacious against *Tænia* as well as against *Bothriocephalus.*

Aspidium, or male fern, has repeatedly given rise to toxic symptoms and death has occasionally followed its use. It is apparently inferior to pome-

granate in the treatment of tenia, and there seems to be little reason for giving it the preference.

Filicic acid was formerly regarded as the active principle; however, it seems that there are a number of principles which share the action.

Pumpkin seed enjoys some reputation as a teniafuge, but it is not often prescribed alone. It has, at least, the advantage of not being toxic to the patient.

SOME OFFICIAL SUBSTANCES USED AS TENIAFUGES.

ASPIDIUM.—U. S. P.—Aspidium, or male fern, the dried rhizome of *Dryopteris Filix-mas* or of *Dryopteris marginalis,* was known to Dioscorides, and advocated by him as being an efficient remedy for tape worm, but fell into disuse and was subsequently nearly forgotten until revived as a secret remedy, for the same parasite, about the middle of the eighteenth century.

Average dose: 4 gm. (60 grains).

OLEORESINA ASPIDII.—U. S. P.—Oleoresin of Aspidium is now directed to be made with acetone. This preparation was first suggested by Peschier of Geneva, about 1825, and has gradually displaced the other preparations of male fern.

Average dose: 2 gm. (30 grains).

GRANATUM.—U. S. P.—Pomegranate, the bark of the stem and root of *Punica Granatum,* was also known to the ancients as a remedy for tape worm. It appears to have been completely forgotten and was introduced into Europe from India during the first decade of the nineteenth century.

Average dose: 2 gm. (30 grains).

FLUIDEXTRACTUM GRANATI.—U. S. P.—Fluid-extract of Pomegranate is made with a menstruum of diluted alcohol containing 10 per cent. of glycerin.

This is a new addition to the Pharmacopeia and has not as yet been widely used.

Average dose: 2 c.c. (30 minims).

PELLETIERINÆ TANNAS.—U. S. P.—Pelletierin Tannate is officially described as a mixture, in varying proportions, of the tannates of four alkaloids (punicin, iso-punicin, methyl-punicin and pseudo-punicin) obtained from *Punica Granatum.*

Average dose: 0.25 gm. (4 grains).

CUSSO.—U. S. P.—Kousso, also known as kosso, koso and Brayera, consists of the dried panicles of the pistillate flowers of *Hagenia abyssinica.* It was discovered by Bruce, about 1768, but was not generally known as an anthelmintic until after Brayer, in 1822, published his observations on the use of the drug in Constantinople. Kousso is usually administered in the form of an unstrained infusion, the object being to secure mechanical irritation by the hairs which are found on the flowers, but they probably play only a minor part in the action of the drug.

Average dose: 16 gm. (240 grains).

PEPO.—U. S. P.—Pepo, or pumpkin seed, the ripe seed of *Cucurbita Pepo,* is usually administered in the form of ground seed, deprived of the hull, or as an emulsion, prepared from the ground seed.

Average dose: 30 gm. (1 ounce).

The tannate of pelletierin, being slightly soluble, is preferred as a teniafuge, but it is some-

what expensive, and the decoction of the root bark is, therefore, frequently directed. It has been suggested that the alkaloid, being volatile, is driven off in the process of boiling, but the loss in this way has proved to be unimportant. The fresh bark is much more efficacious than that which has been kept for some time. It is stated that the deterioration is due to chemical change that takes place in the alkaloid.

As we have no means of knowing the quality of the bark which will be used in making the decoction, it is better to use the pelletierin tannate or to direct the preparation of the extract[1] made according to a formula devised by von Schroeder to enable one to get a fairly uniform product regardless of the quality of the bark used.

About one gram or less of the extract, together with one or two grams of tannin, constitute the ordinary dose for tape worm.

Pomegranate root bark contains a large amount of tannin, too much, in fact, considering the amount of bark required to yield the requisite amount of pelletierin, hence none has to be added to the decoction. So abundant is the tannin that it may cause vomiting and defeat the purpose for which the dose is given, hence the extract mentioned has a decided advantage over the decoction.

1. The ground bark is exhausted by heating with water on a water bath for an hour, the decoction is cooled, milk of lime is added in excess, the mixture filtered, water being added to the precipitate to wash out the alkaloid, the washings added to the filtrate, the filtrate neutralized with dilute sulphuric acid and again filtered. It may be taken in this form, after adding about a gram of tannin, or the neutralized filtrate may be evaporated on a water bath until nearly solid, and then extracted with 70 per cent. alcohol; this is then filtered and subsequently evaporated to a dry extract which is approximately equal to pelletierin.

The following is the method of using pelletierin tannate, the extract described above, or the decoction: Beginning in the evening the patient takes a light meal, which should be exclusively of carbohydrates, and then a laxative; on the following morning, while fasting, he takes 0.4 to 0.5 gm. (6 to 8 grains) of pelletierin tannate, or a corresponding amount of the extract or decoction, followed in half an hour or two hours by a brisk purgative, such as castor oil or syrup of senna.

Of 33 cases treated in this way, the entire parasite, including the head, was removed in 29 cases. Failure in some cases is to be attributed to the head being securely protected by the folds of the mucous membrane.

It is somewhat significant that the many formulas which have acquired some reputation in the treatment of tape worm contain pomegranate bark. The following taken from Osler is almost identical with a formula which has been held as a proprietary by a southern firm for a great many years, among whose patrons it enjoys a considerable reputation:

℞.	Granati	ʒiv	15
	Peponis	℥i	30
	Ergotæ pulveris	ʒi	4
	Aquæ bull.	f℥x	300

An infusion is directed to be made (a decoction is better) from which is formed an emulsion, by adding

	Oleoresinæ aspidii	ʒi	4
	Olei tiglii	mii	12
	Acaciæ, q. s.		

The oleoresin of aspidium may be given as an emulsion or in capsules, or it may be combined

with teniafuges, somewhat after the formula given above.

Pumpkin seeds are harmless and may be given either in substance or in the form of a decoction, using an ounce or more of the bruised seed.

Of the other official substances that have been used to assist in expelling tenia it will suffice to enumerate: ether, chloroform, rectified oil of turpentine, napthalen and thymol. These are all comparatively active drugs and must, therefore, be used with caution.

ANTIGONORRHEICS.

The title antigonorrheics would appear to suggest that we have medicaments that have a specific action on gonorrhea, or the causative factor of that disease, instead of representing, as it really does, a somewhat meaningless array of substances that have been used more or less empirically as remedies for gonorrhea.

The name gonorrhea should properly be reserved for the contagious inflammation of mucous membranes caused by a specific organism, the gonococcus of Neisser. In an even more restricted sense it is now frequently applied to the specific inflammation caused by that micro-organism in the male urethra.

Prior to the discovery of the gonococcus, by Neisser, in 1879, there was probably no one common disease about which there existed such widely varying theories and opinions, and certain it is that no known disease has been so persistently and so widely maltreated.

From the time of the early Greeks and of the

Romans the treatment of gonorrhea appears to have been relegated to the incompetent, the charlatan and the quack, and it may be safely asserted that no one disease, with the possible exception of syphilis, has been the direct, or the indirect, cause of more misery, more suffering and more untimely deaths because of this neglect and maltreatment.

Recognizing the seriousness of the disorder, it would be futile to give suggestions for exhaustive treatment, and practically the only apology that we have to offer for introducing even a mention of the disease, and of some of the official remedies that may be of use in its treatment, is to be found in the fact that victims of this disorder are even now subjects for neglect and malpractice. Evident proof of this can be found in almost any one of the daily papers which regularly advertise specific cures for all forms and kinds of urethral discharges.

The heinousness of this practice, and the really far-reaching and serious consequences of the practice in its ultimate results have not as yet been properly appreciated even by such members of the medical profession as should be more thoroughly well informed. This is, in a measure, evidenced by the recently published statement, made by a prominent genito-urinary specialist, that he frequently uses and recommends a popularly advertised nostrum, the manufacturers of which deliberately mislead the layman into believing that he can be cured in 48 hours.

As suggested above, the treatment of gonorrhea is not by any means the simple procedure that might be wished for and even the differentiation

of true gonorrhea from a non-specific inflammation is one that requires more than ordinary skill and experience, and should, wherever possible, be entrusted to a safe and conscientious specialist, who not alone has the interest of the patient in mind, but who will also attempt, so far as in him lies, to prevent the spread of the infection by impressing on the patient the advisability of observing certain necessary rules of cleanliness, decency and abstinence.

Using the name, gonorrhea, in its most restricted sense, as applying only to the specific urethritis in the male, we may consider this as a type, and recount some of the suggestions for treatment that have been made in connection with it.

This type of gonorrhea is said to be acute, subacute, or chronic, according to the stage of the inflammatory process, and it may involve the anterior urethra alone or include, by continuity, the posterior urethra.

The generally accepted routine treatment is to use only a mild astringent and antiseptic local application for the first or acute stage, to supplement this with the internal use of diuretics, of a terebinthinate or resinous nature, in the subacute or secondary stage, and to use more active astringents and antiseptics as local applications in the chronic stage of the disease.

It will be noted by this that what is usually referred to as an antigonorrheic is in reality, but a diuretic, an antiseptic or an astringent.

Of the several official drugs and preparations that have been found to be more particularly use-

ful in these several stages of the disease, we may enumerate:

POTASSII PERMANGANAS.—U. S. P.—This is recommended to be used, as an irrigation, in very dilute solutions (1-2000 to 1-6000).

ARGENTI NITRAS.—U. S. P.—This was formerly quite popular, in very dilute solutions, but has fallen into disuse and is now frequently substituted by one or the other of the non-official so-called organic silver salts. These latter preparations, while unduly numerous, are usually expensive and the more popular of them are inexpressibly filthy.

A satisfactory and apparently efficient substitute for the several silver preparations has been found in silver iodid. Drs. Siter and Uhle[2] have reported a series of cases in which this preparation was used, in the form of an emulsion of the freshly prepared silver iodid, with excellent results.

A preparation such as was used by Drs. Siter and Uhle may be prepared by any pharmacist, as follows:

Argenti nitratis		2
Potassii iodidi, āā.....gr. xxxiii	2	
Mucilaginis chondri N. F.....f℥vi	25	
Aquæ dest., q. s. ad.....f℥iii	100	

M. Sig.: Use as an injection.

The best method of preparing a finely divided precipitate is to dissolve the potassium iodid in all of the water and add the crystals of silver nitrate gradually, shaking well after each addition; when the silver nitrate is dissolved, add the mucilage and shake thoroughly once more.

The resulting mixture will represent approxi-

2. University of Pennsylvania Med. Bull May, 1905.

mately 3 per cent. of silver iodid. The strength may be increased or decreased as desired. If prepared in this way, the weaker mixtures will require a correspondingly smaller amount of mucilage to hold the powder in suspension and mixtures below 1 per cent. may be dispensed without the addition of any foreign material.

Of the drugs that are frequently used for internal administration in the second or sub-acute stage of the disease the Pharmacopeia includes, in the order of their present popularity:

OLEUM SANTALI.—U. S. P.—Oil of Santal, or oil of sandalwood, is a volatile oil distilled from the wood of *Santalum album.* The Pharmacopeia directs that this oil contain not less than 90 per cent. of santal. This requirement is readily met by the better grades of oil of santal now on the market, so that there is little or no need to resort to proprietary specialties containing, or purporting to contain, true oil of santal.

Average dose: 0.5 c.c. (8 minims).

COPAIBA.—U. S. P.—Copaiba, balsam of copaiba, as it is more popularly called, is derived from one or more South American species of copaiba. It was introduced into Europe by the Portuguese, during the latter half of the seventeenth century, and has long enjoyed the reputation of being of especial use in connection with specific urethritis in the male.

Average dose: 1 c.c. (15 minims).

OLEUM COPAIBÆ.—U. S. P.—Oil of Copaiba is officially described as a volatile oil distilled from copaiba.

Average dose: 0.5 c.c. (8 minims).

OLEORESINA CUBEBÆ.—U. S. P.—Oleoresin of Cubeb represents the alcohol soluble portion of the dried, unripe fruit of *Piper Cubeba.*

Average dose: 0.5 gm. (7½ grains).

OLEUM CUBEBÆ.—U. S. P.—Oil of Cubeb is a volatile oil distilled from cubeb.

Average dose: 0.5 c.c. (8 minims).

Of the more active astringents that are used in the third, or chronic, stage of gonorrhea, in the male, and form such a prominent part in the treatment of the more common form of gonorrhea in the female, we may enumerate:

ZINCI SULPHAS.—U. S. P.—Zinc Sulphate.

ZINCI ACETAS.—U. S. P.—Zinc Acetate.

ZINCI CHLORIDUM.—U. S. P.—Zinc Chlorid.

ZINCI PHENOLSULPHONAS.—U. S. P.—Zinc Phenolsulphonate.

PLUMBI ACETAS.—U. S. P.

ALUMEN.—U. S. P.

ACIDUM TANNICUM.—U. S. P.—Tannic Acid.

ARGENTI NITRAS.—U. S. P.—Silver Nitrate.

BISMUTHI SUBCARBONAS.—U. S. P.

BISMUTHI SUBNITRAS.—U. S. P.

These several astringents, with or without the addition of well-known antiseptics, such as boric acid, phenol, thymol, glycerin, and the several combinations or preparations of them, practically constitute all that is necessary in the treatment of the most persistent of the chronic forms of gonorrhea.

CHAPTER XX.

SUBSTANCES USED AS VEHICLES.

Of the several methods of administering medicines, for their general effect, the administration of liquids by mouth is undoubtedly the most important, as well as the one most generally followed. This one fact alone will suffice as an apology for devoting a separate chapter to the consideration of substances used as vehicles.

The great majority of physicians pay all too little attention to the art of rendering their prescriptions pleasing alike to the eye and to the palate. Even in medical schools, if the matter is considered at all, it is usually deemed sufficient to instruct the student to give the mixture a sweet taste, by the addition of syrup, or a distinctive aroma by the addition of one or the other official medicated water, ignoring entirely individual taste or the nature of the mixture. In the matter of appearance it is commonly considered quite sufficient to avoid the inky mixtures produced by the addition of iron compounds to preparations containing tannin or tannin-like substances.

From the point of view of the patient it is safe to say that the appearance of a mixture is often of even greater importance than the taste, not alone in so far as it concerns the individual preference of the patient, but even to the extent of affecting the ingestion and the subsequent absorption of the medicine, since we know that the digestive se-

cretions are stimulated by tempting looking substances and are inhibited by those which appear disgusting. In the case of women and children the subjects of flavoring and coloring are of much more importance than with men. While the average physician will, no doubt, rightly consider that this subject does not deserve very extensive study on his part, he must admit that the observance of a few easily acquired rules may well be worth remembering.

Unlike the question of ready-made formulas for a great variety of conditions demanding individual consideration, there is no reason why flavoring and coloring should not be reduced to the very simplest forms and used as a routine whenever the mixture admits of it.

When considering a subject that is so far-reaching and varied as this must be, it will, of course, be evident that the discussion of the several matters can not be taken up in detail, but must of necessity be more in the nature of suggestions for observation and study. With the wealth of material that is available, by the use of the official aromatics and diluents, it should be a comparatively easy matter for a physician to become thoroughly familiar with the properties and possible uses of at least several of these preparations and by judicious combination to produce not alone a variety of mixtures, but, also, to impart to them an individuality in which he may well take pride.

Many of the comparatively tasteless substances require but the addition of some mildly aromatic solvent or diluent, such as the aromatic medicated waters. Substances that are more acrid, bitter or

saline in taste may be masked by the addition of syrup to the aromatic, or by the addition of a preparation containing glycyrrhizin, like the now official elixir adjuvans. Nauseous bitters are best masked with strong aromatics and syrup. The simple but persistent bitters, such as quinin and strychnin, are agreeably modified by such an aromatic as tincture of sweet orange peel, wine and sufficient syrup or glycerin to suggest sweetness. As an example of such a preparation we may mention the bitter wine of iron, which will be appreciated if one will but taste this really elegant preparation.

SIMPLE VEHICLES.

The official substances that can be classed as simple vehicles are so thoroughly well known that it may be thought superfluous even to enumerate them. In the order of their importance they are:

AQUA.—U. S. P.

AQUA DESTILLATA.—U. S. P.

SYRUPUS.—U. S. P.

GLYCERINUM.—U. S. P.—Glycerin has been discussed and must be admitted to have medicinal qualities, but, largely on account of its properties as a solvent and because of its sweetish taste, it is frequently used as a vehicle in place of syrup.

MEDICATED WATERS.

Among the more frequently used, and, therefore, the more readily available of the official diluents or vehicles, we class the aromatic, medicated waters. They are particularly well adapted for dissolving such comparatively mild tasting substances

as potassium citrate, sodium benzoate, sodium salicylate, morphin sulphate and antipyrin.

One of the most pleasant of these preparations is:

AQUA AMYGDALÆ AMARÆ.—U. S. P.—Bitter almond water. This contains about 0.1 per cent. of oil of bitter almond, and appears to be particularly adapted for use with sedative expectorants such as codein sulphate.

Average dose: 4 c.c. (1 fluidram).

The following are particularly well adapted for use with children:

AQUA ANISI.—U. S. P.—Anise Water and

AQUA FŒNICULI.—U. S. P.—Fennel Water. They contain about 0.2 per cent. of the respective volatile oils and have long been popular as correctives or diluents for medicines such as fever mixtures and mild anti-diarrhea mixtures, designed primarily for children.

Average dose of either of the above: 16 c.c. (4 fluidrams).

Another aromatic water that has met with considerable use is:

AQUA CINNAMOMI. — U. S. P. — Cinnamon Water also represents approximately 0.2 per cent. of the volatile oil and, as a flavor, is sometimes preferred.

Average dose: 16 c.c. (4 fluidrams).

By far the most popular of the aromatic waters are:

AQUA MENTHÆ PIPERITÆ.—U. S. P.—Peppermint Water and

AQUA MENTHÆ VIRIDIS.—U. S. P.—Spearmint Water. These, like the preceding, are simple solu-

tions of volatile oils in water and represent approximately 0.2 per cent. of their respective volatile oils.

Average dose of either: 16 c.c. (4 fluidrams).

Peppermint water, or spearmint water, is particularly well adapted for use with the mild alkalies, such as potassium bicarbonate or sodium bicarbonate, or mixtures of these with other soluble salts.

The efficiency of solutions of the alkaline bicarbonates may be usually enhanced by the addition of a simple bitter, such as tincture of nux vomica or tincture of calumba.

Simple solutions, even such as contain a small addition of a bitter substance, should be directed to be filtered, as this adds materially to the appearance of the mixture and thus enhances its palatability and efficiency.

When a vehicle having more pronounced characteristics is desired the official aromatic elixir will probably serve to meet more possible indications than any other preparation. It may itself be varied by the addition of the fluid extract of glycyrrhiza, as in the official elixir adjuvans, or by the addition of one of the official spirits, syrups, aromatic tinctures, medicated waters or simple wines.

Aromatic elixir is particularly useful in connection with the scale salts of iron, the bitter alkaloids, and also with the soluble iodids and bromids; with the latter, however, the stimulating effect of the contained alcohol should not be lost sight of.

The following are among the preparations that will be found to be of use in connection with the

possible modifications of the simple elixir or other desirable vehicles:

ELIXIR AROMATICUM.—U. S. P.—Aromatic Elixir is practically a solution of a mixture of the oils of orange peel, lemon, coriander and anise in 25 per cent. alcohol, containing about 38 per cent. of syrup. The resulting preparation is not alone strongly aromatic, but is also sufficiently dense to hold finely divided substances well in suspension, while the alcohol content is not sufficient to be objectionable in the ordinary doses.

ELIXIR ADJUVANS.—U. S. P.—Adjuvant elixir. This is a simple mixture of 12 parts of fluidextract of glycyrrhiza with 88 parts of aromatic elixir, and is particularly well adapted for masking acrid, bitter or saline materials. The contained glycyrrhizin, not being soluble in acid solutions, the preparation is obviously not suited for use with diluted acids or acid salts.

The official spirits that may be used as additions to aromatic elixirs or as correctives to other alcoholic or hydro-alcoholic solutions are:

SPIRITUS ANISI.—U. S. P.—Spirit of Anise contains 10 per cent. of oil of anise in alcohol.

Average dose: 4 c.c. (1 fluidram).

SPIRITUS AMYGDALÆ AMARÆ.—U. S. P.—Spirit of Bitter Almonds contains 10 per cent. of oil of bitter almond in alcohol, and is the most potent of the official spirits. It is markedly aromatic and a very small quantity usually suffices to impart a distinctive almond odor and taste.

Average dose: 0.5 c.c. (8 minims).

SPIRITUS CINNAMOMI — U. S. P. — Spirit of Cinnamon contains 10 per cent. of oil of cinnamon.

Average dose: 2 c.c. (30 minims).

SPIRITUS GAULTHERIÆ.—U. S. P.—Spirit of Gaultheria is a useful preparation for cases in which the patient appears to have a predilection for teaberry or wintergreen. This preparation imparts a distinctive odor and taste and should be used with discretion, as it appears to be objectionable to many people. It represents 10 per cent. of oil of gaultheria.

Average dose: 2 c.c. (30 minims).

SPIRITUS MENTHÆ PIPERITÆ. — U. S. P. — Spirit of Peppermint and

SPIRITUS MENTHÆ VIRIDUS.—U. S. P.—Spirit of Spearmint, in addition to containing 10 per cent. of the respective volatile oils also represent the alcohol-soluble portion of 1 per cent. of the respective dry crude drug, which imparts to them a distinctive yellowish-green color.

Average dose (either): 2 c.c. (30 minims).

The aromatic tinctures that are particularly useful for adding distinctive characteristics to liquid mixtures are:

TINCTURA AURANTII DULCIS.—U. S. P.—Tincture of Sweet Orange Peel. This preparation is directed to be made from fresh peel and represents approximately 50 per cent. of the crude drug. It is a delicate but efficient aromatic and is useful in connection with any of the hydro-alcoholic mixtures.

Average dose: 4 c.c. (1 fluidram).

TINCTURA LIMONIS CORTICIS.—U. S. P.—This is made from fresh lemon peel and, by some, is preferred to orange.

TINCTURA CARDAMOMI.—U. S. P.—Tincture of Cardamom represents 20 per cent. of cardamom in diluted alcohol.

Average dose: 4 c.c. (1 fluidram).

TINCTURA CARDAMOMI COMPOSITA.—U. S. P. Compound Tincture of Cardamom represents 2.5 parts each of cardamom and Saigon cinnamon, 1 part of caraway, 0.5 parts of cochineal and 5 parts of glycerin in sufficient diluted alcohol to make 100 parts.

Average dose: 4 c.c. (1 fluidram).

TINCTURA LAVANDULÆ COMPOSITA.—U. S. P. Compound Tincture of Lavender consists of a mixture of 0.8 parts of oil of lavender flowers and 0.2 parts of oil of rosemary in 75 per cent. alcohol, which is used to exhaust 2 parts of Saigon cinnamon, 0.5 parts of cloves, 1 part of nutmeg and 1 part of red saunders.

The possible uses of this preparation are probably best illustrated by the official solution of potassium arsenite, which is flavored and at the same time colored by the use of 3 per cent. of this tincture.

Average dose: 2 c.c. (30 minims).

TINCTURA VANILLÆ.—U. S. P.—Tincture of Vanilla represents 10 per cent. of vanilla in 65 per cent. alcohol and is sweetened by the addition of 20 per cent., by weight, of sugar.

The official simple wines are:

VINUM ALBUM.—U. S. P.—White Wine. This is an alcoholic liquid, made by fermenting the

juice of fresh grapes, the fruit of *Vitis vinifera,* and usually contains about 10 per cent. of alcohol.

White wine constitutes an excellent vehicle for a number of acrid or bitter substances, and is particularly useful as an addition to the official aromatic elixir. If from 10 to 25 per cent. of white wine be added to aromatic elixir it will impart to the latter a distinctive and generally agreeable odor and taste.

VINUM RUBRUM.—U. S. P.—Red Wine is an alcoholic liquid that is made by fermenting the juice of fresh, red-colored grapes, the fruit of *Vitis vinifera,* in the presence of their skins, and subjected to the usual cellar treatment for fining and aging.

The official syrups that are generally well known or widely used as diluents, correctives or vehicles are:

SYRUPUS ACIDI CITRICI.—U. S. P.—Syrup of Citric Acid. This is a slightly acid syrup, flavored with tincture of fresh lemon peel, and is useful in connection with the aqueous solutions of the alkaline salts of organic acids, such as potassium citrate.

SYRUPUS AURANTII. — U. S. P. — Syrup of Orange also contains a trace of citric acid and has a pleasant acidulous taste. It is frequently used in place of the syrup of citric acid and is preferred by many.

One objection that may be raised to both of these official syrups is that they contain citric acid and are, therefore, incompatible with the carbonates and bicarbonates. Where a lemon or orange flavor is desired, without the citric acid, it

may be secured by adding about 1 per cent. of the corresponding tincture to simple syrup.

SYRUPUS PRUNI VIRGINIANÆ.—U. S. P.—Syrup of Wild Cherry, while it represents the aqueous extractive of 15 parts of wild cherry, is most largely used as a pleasant vehicle or as an addition to other diluents, particularly in connection with expectorants.

Average dose: 4 c.c. (1 fluidram).

SYRUPUS TOLUTANUS.—U. S. P.—Syrup of Tolu represents the water-soluble portion of 5 per cent. of tincture of tolu, and, like the preceding, is frequently used as a corrective in mixtures that are designed for use as expectorants.

Average dose: 16 c.c. (4 fluidrams).

SYRUPUS SARSAPARILLÆ COMPOSITUS.—U. S. P.—Compound Syrup of Sarsaparilla contains fluidextract of sarsaparilla, fluidextract of glycyrrhiza and fluidextract of senna, and is flavored with a mixture of the volatile oils of sassafras, anise and gaultheria.

This preparation constitutes an interesting reminder of the widespread use of sarsaparilla as a universal panacea almost a century ago, but it is now seldom used for any other purpose than as a vehicle. It is particularly useful for such acrid drugs as the soluble mercurial salts and the iodids and bromids.

Average dose: 16 c.c. (4 fluidrams).

For use with immiscible liquids, for making emulsions and for suspending insoluble powders in aqueous solutions it is an almost universal practice to use the official mucilages or gums.

MUCILAGO ACACIÆ.—U. S. P.—Mucilage of Acacia, containing 34 per cent. by weight of acacia, 33 per cent. of limewater and 33 per cent. of distilled water, is probably the best known of these several preparations. It has a very wide field of usefulness, but as acacia is precipitated by alcohol it is not useful in connection with strongly alcoholic liquids. The presence of limewater may prove to be a disturbing factor in connection with solutions of the alkaloids, and here the mucilage may readily be substituted by the syrup.

SYRUPUS ACACIÆ.—U. S. P.—This represents 10 parts of acacia in a moderately heavy syrup.

MUCILAGO TRAGACANTHÆ.—U. S. P.—Mucilage of Tragacanth contains 6 parts of tragacanth, 18 parts of glycerin and sufficient water to make 100 parts. This preparation is particularly useful in connection with alcoholic liquids and is very widely used for suspending the content of resinous tinctures in aqueous mixtures.

Another preparation that is quite extensively used to mask acrid, bitter or otherwise disagreeable drugs is the recently admitted

EXTRACTUM MALTI.—U. S. P.—Extract of Malt occurs as a semi-solid extract, having the consistency of thick honey, and is itself considered to be nutritive, tonic and laxative. It has been used quite extensively, particularly in connection with several widely used proprietary preparations, as a vehicle for cod-liver oil, cascara sagrada and the bitter alkaloids like quinin and strychnin.

Average dose: 16 c.c. (4 fluidrams).

SUGGESTIVE COLORING.

The subject of coloring is a much simpler one than is that of flavoring, but it is of almost equal importance, if we are to judge by the practices that have been followed by manufacturers of elegant proprietaries for upward of a quarter of a century.

Coloring agents are primarily divided into such as are useful with alkaline and neutral substances and such as are useful with dilute solutions of the official acids and acid salts.

For those of the first class, preparations containing carmin or cochineal, for red, and glycyrrhizin for brown are readily available. For the solutions of acids and acid salts, however, neither of these substances would answer, as they are both precipitated by acids, and we have recourse, therefore, to cudbear for the red and caramel for the brown.

Taking the official aromatic elixir as a type, this may be colored a bright red by the addition of from 10 to 20 per cent. of the compound tincture of cardamom, containing cochineal, or it may be given an equally bright red color by the addition of 1 per cent. of the Tincture of Cudbear of the National Formulary. Cudbear is the source of the bright red color that is so common in proprietary preparations, and as cudbear itself has no known medicinal properties, apart from the pleasing suggestiveness of the resulting preparation, we must naturally conclude that the manufacturers of proprietary preparations have succeeded in impressing not alone the patient, but, in many cases at least, the physician also, by the judicious use of pretty colors.

The use of caramel (burnt sugar) is too well known to need further comment, apart from the fact that the National Formulary contains a formula for a compound tincture of cudbear, Tinctura Persionis Composita N. F., which contains 10 per cent. of caramel and will be found useful when a bright brown preparation is desired. From 1 to 5 per cent. will suffice to give a light to dark brown tint to a colorless fluid.

A very pleasing golden-yellow mixture that appears to be fairly stable with either acid or alkaline solutions may be obtained by adding 1 per cent. or even less of the now official tincture of hydrastis. This preparation, though made with 65 per cent. alcohol, mixes readily with the official elixir, but precipitates slightly when added to aqueous solutions, and they should, therefore, be directed to be filtered before being dispensed.

For alkaline or neutral solutions, either aqueous or alcoholic, a bright red color may be obtained by the use of 1 per cent. of Liquor Coccineus, N. F., or from one-tenth to one-fifth this quantity of Liquor Carmini, N. F.

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